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MAIN CONTENTS:

	PAGES
Sleeping Sickness in Tanganyika Territory, 1922–1926...	1–17
Summary of Recent Abstracts. I. Cholera	17–19
Rabies	19–20
Malaria	20–50
Trypanosomiasis	50–55
Leishmaniasis...	55–57
Fevers of the Typhus Group...	57–72
Yellow Fever	72–73
Dengue and Allied Fevers ...	73–74
Plague	74
Cholera	74–76
Amoebiasis and Intestinal Protozoal Infections ...	76–85
Relapsing Fever and other Spirochaetoses	85–87
Yaws	87–90
Leprosy	91–92
Helminthiasis	92–104
Deficiency Diseases	104
Sprue	105–107
Haematology	107–108
Venoms and Antivenenes ...	108–110
Dermatology and Fungus Diseases	110–111
Heat Stroke and Allied Conditions	112
Tropical Ulcer	112–113
Miscellaneous Diseases ...	113–116
Protozoology: General ...	116–117
Entomology and Insecticides: General	117–122
Reports, Surveys and Miscellaneous Papers	122–126

For detailed Contents see pp. ii, iv, vi, viii and x.

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BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES BULLETIN

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SLEEPING SICKNESS IN TANGANYIKA TERRITORY, 1922–1946

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Contents PAGE

1. Historical ... 1
2. The Tsetse Flies Present ... 2
3. The Recent Outbreaks of Sleeping Sickness due to *Trypanosoma rhodesiense* ... 4
4. Treatment ... 7
5. Control Measures ... 7
6. The Sex Incidence of the Disease ... 10
7. Variation in the Incidence of the disease :—
   a. Monthly variation ... 11
   b. Yearly variation ... 11
8. The Rôle of Game ... 14

1. *Historical*

The epidemic of *T. gambiense* sleeping sickness which occurred in Uganda in the early years of the present century gradually spread down both sides of Lake Victoria and invaded German East Africa (now Tanganyika Territory). In 1907, the Germans established sleeping sickness camps at Kigarama, on the west shore of Lake Victoria just south of the Uganda border, and at Shirati on the east side, near the Kenya border [*Sleeping Sickness Bulletin*, 1909, v. 1, 243]. In 1908, cases of sleeping sickness were discovered on Ukerewe Island, at the south of the Lake, and on the Islands of Bumbire and Iroba near the eastern shore and on the mainland of Ihangiro opposite to them [*ibid.*, 396]. On Lake Victoria the Germans recorded 1,405 cases of sleeping sickness in 1908–9, and 27 cases in 1912–13 (Maclean, 1927).

By extensive bush clearing, particularly along the River Mori, south of Shirati [*Sleeping Sickness Bulletin*, 1912, v. 4, 244], they appear to have eliminated the tsetse fly and stopped the southward spread of the disease. It was while working in the River Mori area that Kleine (1909) discovered the cyclical transmission of *T. gambiense* by *Glossina palpalis*.

Lake Tanganyika.—Sleeping sickness reached the western (Congo) shore of Lake Tanganyika about 1901 and soon reached the eastern (German) shore, where it quickly spread. The Germans remarked that numbers of Africans,

bearers of trypanosomes, came from the Belgian Congo to German territory; in one caravan of sixteen, ten persons were found to be infected [*Sleeping Sickness Bulletin*, 1909, v. 1, 396].

By 1907, the authorities had established a sleeping sickness camp at Niansa at the north end of the Lake, and they recorded the disease as being present in the northern third of the Lake shore, from Usumbura to the River Malagarasi [*ibid.*, 243]. In October 1908, 1,517 patients were under treatment [*ibid.*, 396], but this number apparently included the Lake Victoria cases as well. Extensive clearings were undertaken, as in the Lake Victoria area.

By 1914, the Germans had had complete success in combating the disease in the Lake Victoria region, but they considered that the most widespread and most dangerous seat of infection was the Lake Tanganyika coast. The principal efforts of the Government were directed towards preventing the introduction of fresh cases, controlling native traffic, and clearing bush. No Africans from German East Africa were allowed to act as porters in the Belgian Congo [this *Bulletin*, 1914, v. 3, 527].

It was while working at Niansa that TAUTE in 1911 showed that *G. morsitans* could transmit trypanosomes cyclically [*Sleeping Sickness Bulletin*, 1911, v. 3, 291], an observation shortly afterwards published independently by KINGHORN [*ibid.*, 391].

MACLEAN (1927) stated that in 1912–13 there were 3,303 cases under observation, but that most of these were from Ruanda-Urundi, now Belgian Mandated Territory (the northern part of Lake Tanganyika). He stated further that cases were found at the Malagarasi Delta by the Belgian authorities during their occupation of Kigoma and Western Ufipa between 1918 and 1921, but that no records were available and the numbers were not known.

South-Eastern Fly-Block.—In 1911, a focus of human trypanosomiasis was discovered on the upper reaches of the River Rovuma in the Songea District [*Sleeping Sickness Bulletin*, 1912, v. 4, 202]. LAMBORN and HOWAT (1936) give a fuller account of this. They quote from an unpublished report by a German, Dr. Woolf (this is, possibly, the Dr. Wolff referred to by Swynnerton, 1923) that early in 1910 an African was found ill with trypanosomiasis. He had come from his village at the junction of the upper Rovuma and Sawasaru (? Sasawara) rivers. After this patient had been discovered, numerous cases of the same disease occurred along the route on which, it was definitely ascertained, he had travelled. In 1911, a segregation camp was established at Sawasaru to deal with the outbreak, and between 1911 and 1913 seventy-two cases were isolated. From this area the disease spread northwards, and in 1917 it had reached the hinterland of Kilwa, having crossed the River Mbemkuru. TAUTE and HUBER (quoted by SWYNNERTON, 1923) stated that the foci of human trypanosomiasis behind Kilwa and Lindi and further south were confined to water-holes and the banks of rivers that were the halting places for Yao labourers passing from the southern infected foci to the Lindi-Kilwa plantations, and that cases did not occur in the surrounding country. TAUTE in 1913 established that the disease in this area was due to *T. rhodesiense* [this *Bulletin*, 1913, v. 1, 513].

It was in the Rovuma area in 1917 that TAUTE and HUBER (1919) inoculated themselves and 129 Africans with six different strains of *T. brucei* derived from four naturally infected horses and two naturally infected mules, without being infected; this experiment was designed to show that *T. brucei* and *T. rhodesiense* were distinct species.

2. *The Tsetse Flies Present*

The large area of Tanganyika Territory which is infested with tsetse flies is shown on the accompanying map.

The distribution of tsetse flies, and the spread of sleeping sickness, in Tanganyika Territory.

The western and eastern fly-blocks are mainly occupied by *Isoberlinia Brachystegia* (*miombo*) woodland carrying *Glossina morsitans*, in which pockets of *G. pallidipes* and *G. brevipalpis* occur. The northern fly blocks are Acacia savannah, the habitat of *G. synnertoni*, with *G. pallidipes* very widespread throughout and *G. brevipalpis* in isolated areas. In one area of Shinyanga, and in two areas near Babati, *G. morsitans* and *G. swynnertoni* overlap, *G. pallidipes* is also present in the last two areas.

G. palpalis fuscipes occurs on the shores of Lake Victoria. MACLEAN (1927) stated that on Lake Tanganyika the whole length of the shore was at one time infested with *G. fuscipes* (now *G. palpalis martini*), and that *G. morsitans* belts actually reached the Lake shore in many places from the Malagarasi delta southwards, and that it was not uncommon to find both these species at the same spot.

G. longipennis occurs from the Kenya border, through Mbulu district, to the south-west of Lake Eyasi. *G. austeni* is present in the coastal belts on the north-east of the Territory, while *G. fuscipleuris* occurs just over the Kenya border.

For the detailed distribution of the various species the reader should consult POTTS (1937), or the tsetse fly map in "The Atlas of the Tanganyika Territory" (1942), issued by the Tanganyika Territory Department of Lands and Mines, Survey Division.

3. *The Recent Outbreaks of Sleeping Sickness due to T. rhodesiense*

In 1922, sleeping sickness of the *T. rhodesiense* type was identified in Maswa District; and up to the end of 1946 a total of 23,955 cases of the disease have been diagnosed microscopically in the Territory. During epidemic periods many more people probably died undiagnosed. The yearly incidence of the cases in the various areas is shown in Appendix I (p. 16), and the spread of the disease over the Territory is illustrated in the map.

Maswa.—At the end of February, 1922, a large number of African deaths were reported from the Maswa fly-block; and investigations by Maclean established the fact that the cause was sleeping sickness, the responsible trypanosome being *T. rhodesiense.* The people were emphatic that the village of Igombe, on the western border of the Maswa fly-block, was an early focus of the disease, and they traced its passage thence from village to village, naming each, until it came to their own neighbourhood (SWYNNERTON, 1923). Swynnerton stated that it was always easy to trace a sequence between any case and preceding cases; going to see the sick, and taking the sick in, seem to have been the commonest sources of infection recognized by the local Africans. There was no indication of new and independent infections; every case appeared to be traceable to contact with sick persons in the presence of tsetse.

Ikoma.—There is constant foot traffic of Africans between Maswa and the hinterland tribes of Musoma District, and in the Ikoma area of Musoma District, where it has become endemic, this disease was first diagnosed in the middle of 1925.

The Western Fly-Block.—The next outbreak of trypanosomiasis, also caused by *T. rhodesiense,* occurred in the Ufipa area of the Western fly-block. The first cases were found in 1924, but MACLEAN (1927) stated that there was ample evidence to show that the disease had been there at least since 1921, and he mentions that European hunters, who visited Ufipa in 1915, reported that a disease resembling sleeping sickness was then present in the forest villages. The information was very vague, and the Africans maintained throughout that the disease was new to them. MACLEAN (1926) also stated that a fatal disease established itself in the village of Tumbu in 1920 or 1921, and his account, illustrated with a map, traces very clearly the spread of the disease from village to village, spreading outwards from Tumbu. By 1924, the whole of the southern part of the fly-block on both sides of the River Rungwa was infected.

The disease spread northwards, reaching the southern and western sides of Tabora by 1926, and north of Tabora in 1927. MACLEAN (1928) observed that of 40 known cases in this area, there was not a single one who did not come within infective range of another case, and he records another instance of spread from village to village. He stated that all the available evidence pointed to a man-fly spread.

Kahama was infected in 1928; and here again MACLEAN (1929a) showed how the disease spread outwards from the villages of Mtema and Msala, where the first cases seem to have occurred.

From Kahama the disease spread (1) northwards into western Mwanza, (2) north-westwards into Biharamulo district and (3) westwards into Kibondo and Kasulu districts, reaching these areas in 1930. The further spread of the

disease was limited by the fact that it had reached the Lake shore on the north, and the open, fly-free country on the boundary of the Belgian Mandated Territory in the west.

There was a steady progression of the disease through this extensive fly-block, with an interval of about two years before each new area was infected, and a further interval of about two years after infection before the disease reached epidemic proportions. Owing to the control measures undertaken, it is not known when the epidemics would have reached their peaks.

Mkalama.—Sleeping sickness was next diagnosed in Mkalama district in 1932. MACLEAN, in an unpublished official report, gives the following history of the first case in this area. A wife had run away with another man, and the husband set out to look for her. In 17 months' travel, he passed through Mwanza, Kahama, Tabora, Ufipa and down to the coast areas, and he then returned home. Within a few weeks he was ill and died, and a few months later a number of cases of sleeping sickness (*T. rhodesiense*) had been diagnosed in his village and in the valley in the immediate neighbourhood.

Ukerewe.—A sharp, but limited, outbreak started in the Ukerewe peninsula of Lake Victoria, in October, 1939 (the hottest month of the year). It is not known how the disease was introduced, but there is frequent traffic of Africans between this area and the infected areas of Maswa and Musoma.

Babati-Kondoa.—In October, 1943 (again the hottest month of the year), cases of sleeping sickness were diagnosed amongst the African labourers working on European farms in the Babati area of the Northern Province. Most of these labourers were aliens from other districts, who had come in search of work; and at least one party of Waha had come from the western part of Kibondo district, and had travelled through the Kibondo-Kahama-Mkalama infested areas before arriving at Babati.

The disease is spreading southwards into the north-western corner of Kondoa-Irangi district. There are records of African inhabitants of Kondoa travelling from Arusha through the Babati area and being diagnosed on their return home; several men, previously healthy but later infected, had been working on bush-clearing at the southern end of the Babati area.

South-Eastern Fly Block.—In December, 1924, an outbreak of the disease occurred in Liwale district, about 50 miles north-east of the district headquarters. This small outbreak was fully described by DYE (1927). In the memory of the older inhabitants the area had a bad reputation; villages built there had sooner or later to be abandoned owing to sickness, which ceased when the inhabitants took up new sites farther away. As, however, the valleys possessed good soil and water in a dry and unprofitable area, the people usually made attempts to return, although certain sites, favourable in themselves, had become definitely banned. That sleeping sickness was well known was shown by the fact that it possessed a local name. Although Dye does not discuss how it was introduced into the area, he was certain that the disease, which had started in the village of Namabao, was spread from village to village by infected human beings. The disease eventually disappeared, apparently as a result of a further spontaneous abandonment of the whole area by the people.

In March, 1936, sleeping sickness was found at Madaba, 100 miles due north of the district headquarters, and the present author obtained the following history. Saidi Idunda, who had lived on the River Mbemkuru for about a year, returned home in September, 1935, began to have fever and died in November, 1935. When he was dying, he was housed by his brother-in-law, Abdullah Likurunju. A short time after Saidi's death, Abdullah fell ill and then his nephew, grand-daughter and his wife also did so, trypanosomes being found in the blood of the last-named in April, 1936. Ali Mbiriri visited Abdullah in January, 1936, before the latter's death, and returned home with

fever and died ; and after his return his father fell ill and trypanosomes were found in his blood. Further patients all gave a history of having lived with or visited one of the above patients. The disease eventually spread widely in the area, cases being diagnosed as far west as the River Mbarangandu, which is the boundary between Liwale and Mahenge district, and a favourite resort of fishermen of both areas.

The River Mbemkuru area was probably infected during the period of the German occupation, when sleeping sickness spread from the Rovuma to Kilwa ; and the disease appears to be endemic there, as cases have been found from 1924 onwards, whenever this inaccessible area has been surveyed. There is no doubt that the 1936 outbreak in Liwale was the direct consequence of the introduction of the disease from this area by an infected human being.

Rufiji.—Only three cases, diagnosed in 1934, 1936 and 1938, have so far been reported in Rufiji district. The last of these is particularly interesting, as the patient had lived in the village of Bagala for over a year. During September, 1938, he had visited the village of Jumbe [sub-chief] Saidi Rupia in Mahenge district, and he fell ill with trypanosomiasis in October, on his return home. To reach Saidi Rupia's village, he would have had to travel through the northern part of the infected Liwale area.

Mahenge.—Isolated cases of trypanosomiasis were recognized in 1925, 1926 and 1930. The last patient was a child 2–3 years old who had visited a village on the Songea road where the local track from Liwale joins the main road.

The first case of the present outbreak, however, was diagnosed in April, 1939. The patient was a Game Scout who had been stationed for some time at the village of Jumbe Saidi Rupia (see above). The next case, in August, was in a mission teacher at Mchombe mission. Three cases were diagnosed in September at the southern edge of the district ; all of the patients gave a history of having visited Liwale district. In November, a hut counter living on the River Kilombero, in the north-western corner of the district, was found to be infected ; and in December, in the same area, a relative of the teacher from Mchombe was diagnosed. The disease subsequently spread all over the southern part of the district, although in the north-west corner it remained localized.

Whether the disease was introduced to the village of Jumbe Saidi Rupia by the Rufiji traveller, or whether the village was already infected by intercourse with the Liwale area, remains unknown. By analogy with the spread of the disease in the western fly-block, with the two years' lapse before successive areas were infested, one would suspect that Saidi Rupia's village was already infected in 1938 from Liwale, and that it was the chief cause of the spread of the disease to Mahenge in 1939.

Southern Province.—Up to 1938, the cases which were recorded in the Southern Province were either in Africans from Portuguese East Africa, or else in local Africans who had visited that country.

When resettlement was taking place in Mahenge in 1940, many of the peoples of the southern part of the district moved into bush villages in Tunduru and Masasi districts, and there was a sharp rise two years later in the number of cases diagnosed in the northern parts of these districts. Some of them, particularly in Masasi district, may also have been infected on the River Mbemkuru.

Lake Tanganyika.—The first cases encountered in this area since the British Administration took over the Territory were found in 1924. Several of them occurred either in natives of the Congo or in others who had recently visited infected areas situated in Belgian territory (TANGANYIKA TERRITORY, *Ann. Med. Report*, 1925, 23). The infection was caused by *T. gambiense*. Since then, sporadic cases were found between the Anglo-Belgian border and Tongwe,

where the disease appeared to be endemic (MACLEAN, 1927, 1930). No cases were found south of this, though a thorough search had been made since October, 1925.

In 1938, cases of sleeping sickness began to be recognized at Karema, and on the southern half of the Lake. The infection of a European Telegraphic Inspector in an area south of Karema led to an extensive examination of the area, when it was found that the infection was of the *rhodesiense* type. This was an extension westwards of the Ufipa outbreak, through the *morsitans* fly belts, until the disease had reached the Lake shore.

A total of thirty-one officials and non-Africans have been infected since 1922. This number is made up of seven European Officers, one Sub-Assistant Surgeon and five African subordinate staff, all Government officials; and ten Missionaries, four miners, two other Europeans and two Asian traders.

4. *Treatment*

MACLEAN and FAIRBAIRN (1932) recorded the results of treatment of 719 cases of *rhodesiense* sleeping sickness; the patients were kept under prolonged observation. In Maswa district, where patients came for treatment relatively late, of 131 patients treated, twenty-one (16 per cent.) were cured after an observation period of more than six and a-half years. In the Tabora (epidemic) area, where patients came for treatment relatively early, of 588 patients treated, two hundred and eighty-three (48·2 per cent.) were well, and probably cured, after an observation period of not less than two years and five months. FAIRBAIRN (1944) has recorded the present methods of treatment; and he has emphasized that a prognosis can only be given if the cerebrospinal fluid protein has been estimated at the beginning of treatment and during an adequate follow-up period.

In any outbreak of sleeping sickness in a new area, the first patients seen are usually at advanced stages, and it takes some months before the results of treatment, and of propaganda, have any effect in making patients come earlier for treatment. The cure rate of 48 per cent. recorded for the Tabora epidemic is about the best one can expect in any large epidemic; and it is considered that a minimum of 11,500 of the 23,955 patients diagnosed between 1922 and 1946 have died, or will die. This is a serious loss to a country which is already under-populated.

5. *Control Measures*

As soon as the disease was found in an area, dispensaries were built, and staffed with properly trained persons, equipped with microscopes; treatment was soon started. Treatment alone, however, can never control or stop an epidemic, and was merely palliative until more positive preventive measures could be planned and put into operation. These control measures were based on the principle of breaking the contact between man and the tsetse fly.

Maswa.—In 1922, approximately 5,000 people were removed from the tsetse bush and resettled in the open country on the edge of the bush. This caused considerable congestion in the open country, but by communal bush-clearing during 1926–28 the congestion was relieved and sufficient land was made available for all the people. Since 1935, only one case (in 1938) has been diagnosed in the district.

Ukerewe.—When the Ukerewe outbreak began, the Tsetse Research Department applied in the field their experimental method of "discriminative bush clearing". This implies the clearing of only those parts of the bush which form the essential tsetse habitat. During 1940–42, 118 square miles were treated, involving the removal of 4,600 acres of hard-pan vegetation, or only 6 per cent. of the total area of bush (BAX, 1943). The tsetse was eliminated in parts, or so

reduced in numbers in other parts, that the outbreak ceased, although the people had remained dispersed in their hamlets.

Babati.—In Babati, the method employed in 1944 was to remove the people and resettle them in open country. A measure of success was obtained, but the open country has not yet been sufficiently enlarged. Many of the cases now being diagnosed occur in people who surreptitiously return to the infested bush to collect the bananas, coffee and pawpaws which had to be left behind when they were resettled.

Remainder of the Territory.—In the remainder of the Territory, the policy adopted by MACLEAN was to make fly-free settlements in the fly-bush. The aim was to have at least 750–1,000 taxpayers in each settlement; the larger figure is preferable, but many of the earlier settlements had considerably less for various administrative reasons. Allowing a family of 3·5 persons per taxpayer, this meant a total population of approximately 2,600–3,500 people in each settlement.

The land selected for resettlement was usually a piece of virgin *miombo*, and it had to be of such size as to allow of 16 acres of good agricultural soil (excluding hills, swamps, etc.) per taxpayer, with adequate water supplies. As the area was a virgin one, and usually heavily covered in bush, it took up to 4 years or more to clear properly the first 4 acres per taxpayer; and it would take up to 12–15 years to clear the whole 16 acres per taxpayer, with all the work being done by an annual turn-out of communal labour. The incidence of the disease was only affected, therefore, about 2–4 years after the people had been resettled. FAIRBAIRN (1943) has given a full account of the details in making these resettlements. Table 1 shows the number of settlements made in each area.

TABLE 1

The number of settlements made, and the number of people moved, in each area.

Area	No. of Settlements	Year resettled	Taxpayers moved	Family per Taxpayer	Total people moved approximately
Maswa ...	to open country	1922			5,000
Ufipa } Tabora }	10	1925/27 1936/37	minimum of 8,640	3·3	28,500
Kahama ...	9	1928/29	1,900	3·3	6,300
Kibondo ... } Kasulu ... }	4 3	1933	13,545	3·3	44,700
Biharamulo ...	5	1933/34	4,113	3·3	13,600
W. Mwanza	6	1934/36	1,541	3·5	5,400
Mahenge ...	9	1941/45	6,497	4·0	26,000
Babati ...	1	1944	420	—	1,372
Liwale ...	1	1945	2,000	—	8,000
Total ...	48		38,656		138,872

Approximately 140,000 people have been removed from isolated bush hamlets and resettled, either in settlements or in open country. By referring to Appendix I, it will be seen that such resettlement had a marked influence on the number of cases of sleeping sickness diagnosed in subsequent years.

Maclean has often been severely criticized for making settlements in the fly-bush, particularly as many of them were 150 miles or more from the railway and administrative headquarters, and the roads to them are often closed for 6 months or more during the rains. But there are a number of points which the critics have overlooked.

Sleeping sickness occurs in a population which is widely dispersed in isolated hamlets in the fly-bush. It is considered that the condition most favourable to an epidemic is a density of population of 5 to 25 taxpayers (*viz.* 16 to 80 people) per square mile. With a density of less than 10 people per square mile the disease can occur, but the population is usually so scattered that the infection is self-limited; while with a density of 100 people or more per square mile, many of the villages are large enough to protect themselves from tsetse by the clearings made for their farms.

By the very nature of things, the people who elect to live in such widely scattered conditions are the most primitive in the Territory. They are the hunters who do little agriculture, or else the malcontents and the very conservative who desire to escape from tribal authority and from the restrictions and controls of progressive administration. MACLEAN (1929b) has ably summarized the position, and his paper should be consulted. Despite their primitive outlook, these very same people have an intense attachment to their tribal lands, and refuse to be moved out of their tribal area. They had, therefore, to be settled on their own land. It was difficult enough for the administrative officers to organize the present settlements; it would have been impossible to make settlements by moving the people right out of their tribal area.

Where a Native Authority had enough people to make one or more settlements of the correct size, these could be sited anywhere within the tribal lands. But where the people concerned were too few to make a settlement on their own, they were usually moved to the boundary of their area and joined up with a settlement of the neighbouring Authority, to make one large area with the tribal boundary running through the settlement.

Even at present, there is some tendency to re-establish bush hamlets, and one of the main reasons for this is the fact that the head of a family moves out of a settlement, usually with the Chief's knowledge and often at his suggestion, to settle on the boundary of the tribal area in order "to guard the frontier" and see that the neighbouring Chief is not encroaching on the tribal lands.

When the Ufipa settlements were made in 1925–26 they were in Ufipa district. The district headquarters was at Nyamanyere (since moved further south to Sumbawanga) in the south-west of the Territory, and the settlements were therefore placed as far south as possible, in order to reduce the distances to be travelled with porters, on inspection and for the disposal of produce. Some years later, the district boundaries were re-aligned, and the Ufipa settlements came under the administration at Tabora in the centre of the Territory and on the railway line. If Tabora had been the administrative headquarters in 1925, the settlements could have been sited at least 50 miles further north and nearer to the railway line, but it was now too late. The same remarks apply to settlements which are now in Chunya district, but which were formerly under administrative charge from Tabora.

Finally, even if the people could have been moved out of the whole of the south-western fly-block and settled on or near the railway line, it would have involved leaving a vast area of country completely uninhabited and unadministered, which was politically undesirable.

In two areas the disease appears to have been completely eradicated—in Maswa by settling the people in open country and in Ukerewe by eliminating the fly by discriminative bush clearing. The soundest control measure would appear to be a combination of the two methods, *i.e.*, settling the people in open country which has been enlarged to receive them, and then discriminative clearing of the bush over a fringe half a mile wide, so that the people visiting the immediate forest for firewood, building poles, grass, etc., would not come in contact with tsetse.

6. *The Sex Incidence of the Disease*

The sex of the patients infected is shown in Table 2, the figures referring to cases diagnosed from 1936 onwards.

TABLE 2

The Sex of Persons suffering from Sleeping Sickness in the various Areas.

Area	Males	Females	Boys (5–15 yrs.)	Girls (5–15 yrs.)	Infants male	Infants female	Totals
Ufipa	733	88	32	9	1 (2 yrs.)	—	863
Tabora	221	34	9	2	—	—	266
Kahama ...	878	156	59	15	1 (3 yrs.)	—	1,109
Western Mwanza	67	10	4	2	—	—	83
Kibondo ...	842	142	36	17	1 (2 yrs.)	2 (3 yrs.)	1,040
Kasulu	217	43	6	—	—	—	266
Biharamulo ...	158	30	2	3	—	—	193
Ikoma (Musoma)	301	126	21	14	—	—	462
Ukerewe ...	172	94	31	16	7 (1–4 yrs.)	1 (4 yrs.)	321
Mkalama ...	53	31	7	5	—	1 (3 yrs.)	97
Babati ...	395	70	10	8	1 (1½ yrs.)	1 (3 yrs.)	485
Kondoa ...	82	47	5	2	1 (2 yrs.)	—	137
Liwale ...	65	55	7	7	1 (2 yrs.)	1 (8 mths.)	136
Mahenge ...	116	64	15	6	2 (2 yrs.; 4 yrs.)	2 (10 mths.; 4 yrs.)	205
Rovuma (S'thern Province)	129	102	13	12	1 (2 yrs.)	2 (3 mths.; 3 yrs.)	259
L. Tanganyika shore	32	12	1	—	—	—	45
	4,461	1,104	258	118	16	10	5,967

In the old settlements of Ufipa, Tabora, Kahama, Western Mwanza, Kibondo, Kasulu and Biharamulo, which were made between 1925 and 1936, there was a marked preponderance of males, the proportion of adult men varying from 79·2 to 85·0 per cent., with only 5 children aged 2–3 years infected in a total of 3,820 cases (0·13 per cent.). In these areas, it is the men who leave the settlements to hunt, to collect beeswax and to transport produce, and they are often accompanied by boys of 12–15 years of age.

On the other hand, in the areas of Ikoma, Ukerewe, Mkalama, Kondoa, Lindi, Mahenge and Southern Province, where epidemic conditions prevailed for a greater part of the period under consideration, the proportion of women was high, varying from 27·3 to 40·4 per cent., with 21 infants and children aged from 3 months to 4 years infected in a total of 1,617 cases (1·3 per cent.). The fly was, therefore, present in the huts and in the immediate surroundings, where the women were at work.

Three infants, 3, 8 and 10 months old, were infected, as well as quite a number of other small children, and the incidence in infants and children would have been greater had the records of the Kahama epidemic of 1928–29 and of the Kibondo epidemic of 1933–34 been available. There was no evidence, in our experience, that infants had any inherited immunity. Whether they were infected or not depended upon the closeness with which they were brought into contact with the fly.

DUKE (1923), in his report on the Maswa epidemic, stated that the majority of the cases seen were in adults, both men and women, and that the disease was rare in young people below the age of fifteen and exceedingly rare in young children. He stated that the age distribution thus corresponded to what

observers in the Congo had learnt to associate with human trypanosomiasis in epidemic, as opposed to endemic, form. In Tanganyika Territory, however, it is characteristic of epidemics that a high proportion of women, children and infants are infected.

7. *Variation in the Incidence of the Disease*

A. *Monthly Variation*

The effect of temperature on the transmissibility of the polymorphic trypanosomes by *Glossina* has long been known. KINGHORN, YORKE and LLOYD (1913) showed that the earlier stages of the development of the trypanosome in the fly could occur at a comparatively low temperature (60°F., 15·6°C.); that the trypanosomes could persist in this stage for at least sixty days without the salivary glands being invaded; but that for the completion of the cycle it was necessary for the temperature to which the flies were subjected to be raised to a considerable extent (75°–85°F., 23.9°–29·4°C.). They also found that the percentage of infected "wild" flies caught in the Luangwa Valley was greater in the hot than in the cold season; and an examination of their Table 13 shows that the highest percentages were found when the mean external shade temperature was 79·0°–87·1°F. (26·1°–30·6°C.), while between 67·2° and 77·5°F. (19·6°–25·3°C.) no infected flies were found. LLOYD (1930) and TAYLOR (1932) had shown that it was possible in the laboratory to obtain greatly increased infection rates by incubating the tsetse flies at 33°–37°C. A more recent finding by BURTT (1946) was that when pupae of *G. morsitans* were incubated at 30°C., the flies that emerged gave much greater transmissibility rates than flies which had come from pupae kept at normal (and lower) laboratory temperatures.

At Tinde Laboratory it has been found that the percentage of flies infected in each month is correlated significantly with the mean maximum temperature to which the flies are exposed. The highest transmissibility rate is obtained in October at the height of the hot, dry season, and the lowest in May–July, in the cool period after the rains.

Table 3 shows the number of cases of sleeping sickness diagnosed in each month, totalled over a period of years, and the average monthly mean maximum temperature recorded at the Meteorological Station, Tabora, for the period 1936–46. Tabora is situated in the centre of the western fly-block, at an altitude of 4,000 feet, and the temperatures recorded there are representative of the whole of the area.

In the western fly-block as a whole there was a very significant correlation between the monthly mean maximum temperature at Tabora and the number of cases of sleeping sickness diagnosed in the following month ($P < \cdot 01$); and this level of significance was maintained when the figures for individual areas were examined, with the single exception of Ufipa. In the Kibondo-Kasulu-Biharamulo areas, taken together, there was also a very significant correlation ($P < \cdot 01$) between the maximum temperature and the number of cases diagnosed *two* months later. This correlation is shown diagrammatically in Fig. 1.

No suitable temperature data were available for comparison with the cases in the remainder of the Territory.

The increase in the number of cases noted in the hot dry season is thus probably due to the combined effects of occupation, leading men into the fly bush, and an increased proportion of infected flies encountered, owing to the high temperatures of that period.

B. *Yearly Variation*

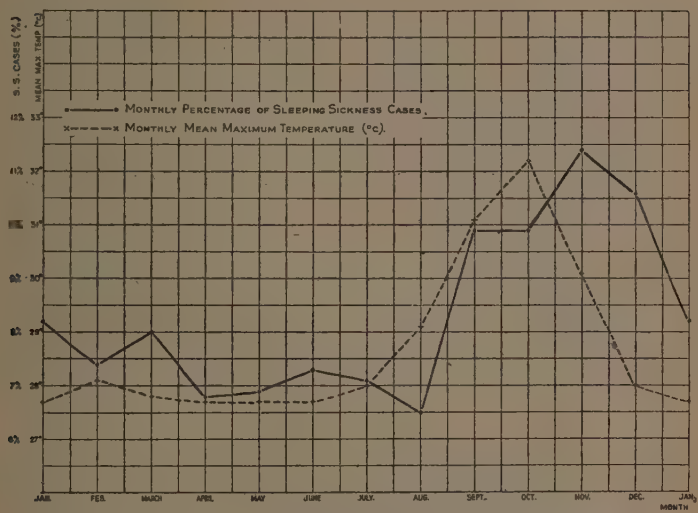
The Tsetse Research Department take as their index of the fly population in the bush the number of old male *G. swynnertoni* caught per 10,000 yards on fly

TABLE 3.

The monthly incidence of cases of Sleeping Sickness.

	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
Ufipa	114	118	136	105	93	91	104	75	62	113	130	176	1,317
Tabora-Nzega ...	134	162	169	112	102	125	127	112	151	210	210	210	1,824
Kahama	325	286	329	333	317	309	332	290	632	487	594	423	4,657
W. Mwanza	31	19	22	15	15	15	12	15	15	11	19	1	190
Kibondo	408	308	320	265	297	346	281	288	372	380	456	493	4,214
Kasulu	33	52	46	37	51	41	42	24	41	64	53	47	531
Biharamulo	20	20	25	19	26	32	27	48	18	21	24	36	316
Average mean maximum temperature° C. Tabora, 1936–46 ...	27·7°	28·1°	27·8°	27·7°	27·7°	27·7°	28·0°	29·1°	31·1°	32·2°	30·1°	28·0°	
Maswa	28	16	24	32	14	15	15	6	20	10	16	25	221
Ikoma	55	80	77	60	76	59	92	95	74	77	81	51	877
Ukerewe	22	31	19	21	26	23	26	16	14	43	40	42	323
Mkalama	6	8	—	4	6	6	11	9	3	13	14	27	107
Babati	34	47	63	37	33	38	31	40	44	46	43	29	485
Kondoa	—	—	1	2	—	3	13	28	25	18	38	16	144
Liwale	30	57	41	44	44	34	33	25	18	20	19	13	378
Mahenge	19	10	15	19	52	36	25	20	20	20	12	18	266
S. Province	12	24	24	30	22	19	24	38	29	15	19	17	273
L. Tanganyika shore	5	4	10	9	4	3	13	8	10	10	8	12	96
Total ...	1,276	1,242	1,321	1,144	1,178	1,195	1,208	1,137	1,548	1,558	1,776	1,636	16,219

FIG. 1.

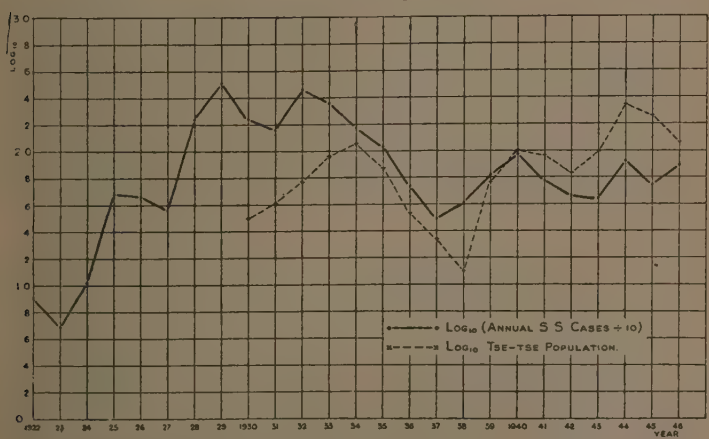


The monthly incidence of cases of sleeping sickness in the Western Fly Block related to the monthly mean temperature at Tabora.

rounds in Shinyanga. The yearly average of these catches is given in Appendix I.

In Fig. 2, which is drawn on a logarithmic scale, the catches of tsetse flies in Shinyanga are shown against the number of cases of sleeping sickness diagnosed in the whole Territory. Statistical analysis shows that, over the period 1930–45, there is a very significant correlation between the two ($P < \cdot 01$). When the year 1946 is included, the correlation is lower, but still significant

FIG. 2.



Logarithmic graph of tsetse population, Shinyanga, and the number of cases of sleeping sickness diagnosed in Tanganyika Territory.

(P nearly equals ·02). The outbreak in Kondoa-Irangi may be responsible for the adverse effect of the 1946 figures on the total correlation. There is a suggestion of a cyclical variation, but the observations are too few.

A study of Appendix I shows that sleeping sickness has usually reached epidemic proportions in new areas in the same years that maximum numbers of cases have occurred in distant endemic centres (which might have a different species of fly); *e.g.*, compare in 1932 Ikoma-Ufipa-Tabora with Kibondo; in 1940, Kibondo with Ukerewe-Mahenge; and in 1944, Kahama-Kibondo with Babati. Further, in the years 1927, 1937–38 and 1942–43 minimal numbers of cases occurred in widely separated areas. The yearly variation in the tsetse population is probably due to a long-term variation in climatic conditions. One of the climatic factors may be temperature, but there are probably other, unknown, factors at work over a long period. The variation in the number of cases of sleeping sickness may be directly correlated with the tsetse population (*i.e.*, the more flies there are the greater the chance there is of being bitten, and hence of more cases). On the other hand, the correlation may be indirect, through climatic conditions influencing both the tsetse population and the infection rate of the fly.

8. *The Rôle of Game*

In the foregoing study of sleeping sickness in Tanganyika Territory, it has been shown that the introduction of the disease into an area can usually be traced to the arrival of a human being infected with *T. rhodesiense*. There is no need to postulate the repeated infection of man with *T. brucei* derived from game. It has been shown, however, that a strain of *T. rhodesiense*, passaged through sheep and antelope by cyclically infected *G. morsitans*, was still infective for man ten and and half years after its removal from man (FAIRBAIRN and BURTT, 1946). The rôle of game is that when once the disease has been introduced into an area the game become infected with *T. rhodesiense*, and they then act as reservoirs for maintaining the disease endemically.

The statement that game act as reservoirs for *T. rhodesiense* has been criticized on the grounds that this has only been demonstrated hitherto in the laboratory, and that *T. rhodesiense* has never been recovered from game in its natural state: but this criticism has been answered.

MACKICHAN (1944) reported an epidemic of Rhodesian sleeping sickness which began in November, 1940, and swept through the Busoga and Samia districts of Uganda. In April, 1943, Dr. C. H. N. Jackson, of the Tsetse Research Department, was working on the insect vector of this epidemic, and he was engaged in collecting tsetse flies in the Lugalla area of the Samia district. The area where the flies were caught had been cleared of all inhabitants at least one year before; the nearest human source of trypanosomes was about 3 miles distant from where the flies were found; and the only persons entering the area were very occasional trespassers in search of fish and game. While collecting the flies, one of Jackson's fly-boys from Tanganyika Territory became infected with sleeping sickness.

The flies caught were fed in batches of 100 on each of fifty clean, laboratory-bred rats, and it was estimated that 3,500 flies fed. When feeding was completed, the flies were killed and examined. One *G. palpalis* was found, and the rat on which this fly had fed was discarded; all the rest of the flies were *G. pallidipes*. Five rats were infected with polymorphic trypanosomes, with incubation periods of 7 days in each case. The five rats were killed, 0·25 cc. of heart blood was mixed with 0·25 cc. of sterile normal saline and injected into the arm of each of five volunteers. Four of the men showed no reaction and their blood was negative up to the 10th day after inoculation, when they were given treatment. On the 4th day, the fifth man developed a painful swelling

at the site of the injection; on the 5th and 6th days his temperature was 102°F.; and on the afternoon of the 6th day scanty trypanosomes were found in his peripheral blood: he was then given treatment. The volunteer was an employee of the Medical Department and lived at Jinja, where he was out of contact with the fly.

This experiment establishes the fact quite clearly that *G. pallidipes* was carrying a polymorphic trypanosome, infective to man and morphologically identical with *T. rhodesiense*. The area was as completely depopulated as anyone is ever likely to find for the purposes of such an experiment; and there is no doubt that the fly could have been infected only by feeding on an animal reservoir of the trypanosome.

Epidemiological evidence that game act as reservoirs for the human disease also comes from two areas in Tanganyika Territory. The River Ugalla, in the Tabora district, was depopulated in 1925–26, and, except for an occasional foot-traveller, there are no human beings in the area during the six months of the wet season. Fifty miles to the east of Kibondo are the native-worked salt deposits of Kimyora, which are only visited (illegally) for 2–3 months at the end of the dry season. In both of these areas cases of sleeping sickness occur as soon as the fishermen return to fish the Ugalla pools in June, or the people of Kibondo district go to the salt deposits in August.

Dr. C. H. N. Jackson, in a personal communication, states that, in the field, the average length of life of male *G. morsitans* varies from about 2 weeks in the hottest time of the year up to 5 or 6 weeks during the rains; the extreme span of life is believed to be about 12 weeks. The female flies live for an average of perhaps 2 months; females living for longer than 4 months are extremely exceptional (see JACKSON, 1944, Table 17). It is not possible for a fly which has been infected from a human being in November of one year to be able to infect a human being in June of the following year. The infected flies which are present in June of any year can only have obtained their infection from any existing game, which were acting as reservoirs of the parasite.

It is, therefore, understandable why the disease has not died out in Tanganyika Territory, although resettlement has controlled its incidence. So long as it is necessary to make settlements in fly-bush containing an abundance of game, visits to or through the bush will be dangerous; and so long as game are present and act as reservoirs of the parasite, the disease can only be reduced in incidence, not eliminated.

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REFERENCES

BAX, S. N. (1943) *East African Agric. J.*, v. 9, 2. [*Trop. Dis. Bull.*, 1944, v. 41, 463.]

BURTT, E. (1946) *Ann. Trop. Med. & Parasit.*, v. 40, 18. [*Trop. Dis. Bull.* 1946, v. 43, 827.]

DUKE, H. L. (1923) *Proc. Roy. Soc.* Ser. B, v. 94, 250. [*Trop. Dis. Bull.*, 1923, v. 20, 309.]

DYE, W. H. (1927) *Trans. Roy. Soc. Trop. Med. & Hyg.*, v. 21, 187. [*Trop. Dis. Bull.* 1928, v. 25, 331.]

FAIRBAIRN, H. (1943) *East African Agric. J.*, v. 9, 17. [*Trop. Dis. Bull.*, 1944, v. 41, 12.

——. (1944) *Tanganyika Territory Medical Department Pamphlet No. 40.* Dar es Salaam: Govt. Printer. [*Trop. Dis. Bull.*, 1945, v. 42, 452.]

——& BURTT, E. (1946) *Ann. Trop. Med. & Parasit.*, v. 40, 270. [*Trop. Dis. Bull.*, 1947, v. 44, 506.]

Appendix 1

The number of cases of Sleeping Sickness diagnosed microscopically in Tanganyika Territory during 1922–1946.

Area	1922	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	1946	Total
Maswa ...	*79	49	28	108	†104	†65	†62	18	10	4	10	14	4	8	—	—	1	—	—	—	—	—	—	—	—	564
Ikoma ...	—	—	—	12	113	*55*	110	125	147	74	**265**	263	178	**190**	103	48	*44*	55	**76**	71	60	27	*23*	33	47	2,119
Ukerewe ...	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	49	‡**177**	‡79	‡18	—	—	—	—	323
L. Tanganyika	—	—	15	17	14	9	4	23	18	26	30	20	—	1	—	—	1	1	1	8	1	32	2	—	—	223
Ufipa ...	—	—	58	*251	*136	**62*	107	76	**266**	169	**209**	130	127	92	64	*29*	77	**190**	115	94	59	*42*	69	52	80	2,554
Tabora ...	—	—	—	8	87	109	495	*891	104	194	**264**	123	175	138	*74	**23*	34	32	**35**	16	15	9	*6*	14	8	2,854
Kahama ...	—	—	—	—	—	—	*948	*2121	1070	500	479	442	254	229	54	*34*	88	**143**	130	91	*74*	80	**161**	107	147	7,152
W. Mwanza	—	—	—	—	—	—	—	—	64	34	**163**	89	*69	*38	*21	*3*	3	10	7	4	4	10	7	9	5	540
Kibondo ...	—	—	—	—	—	—	—	—	} 55	408	**1147**	*835	456	*273	89	79	*66*	87	**173**	116	*83*	90	**129**	84	44	4,214
Kasulu ...	—	—	—	—	—	—	—	—		14	**111**	*70	64	18	3	3	*1*	16	13	15	29	19	52	57	63	548
Biharamulo	—	—	—	—	—	—	—	—	7	26	167	*258	*126	67	15	*4*	6	4	14	25	15	14	24	31	41	844
Mkalama ...	—	—	—	—	—	—	—	—	—	—	18	54	17	17	8	8	9	7	**56**	15	2	4	1	10	10	236
Babati ...	—	—	—	—	—	—	—	—	[1]3	—	—	—	—	—	—	—	—	—	—	—	—	27	*215	86	157	488
Kondoa ...	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4	3	137	144
R. Mbemkuru	—	—	3	—	—	—	—	—	—	—	4	6	4	2	—	—	—	—	—	—	—	—	—	—	—	19
Liwale ...	—	—	—	**78**	2	60	25	4	5	—	—	—	—	—	**102**	75	73	43	35	18	25	13	5	—	—	563
Rufiji ...	—	—	—	—	—	—	—	—	—	—	—	—	1	—	1	—	1	—	—	—	—	—	—	—	—	3
Mahenge ...	—	—	—	2	1	—	—	—	1	—	—	—	—	—	—	—	—	8	**102**	*28	*22	*20	*47	25	12	268
S. Province	—	—	—	—	2	—	—	4	—	—	1	—	—	2	1	—	7	18	9	5	49	52	**80**	35	34	299
Total	79	49	104	**476**	459	*360*	1751	**3262**	1750	1449	**2868**	2304	1475	1075	535	*306*	411	663	**943**	585	456	*439*	**825**	546	785	23,955

	1930	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945	1946
Yearly average of *G. swynnertoni* caught per 10,000 yds. on fly-rounds in Shinyanga	31·6	40·7	58·9	90·4	**113·2**	74·5	34·1	22·1	12·7	57·9	**101·0**	90·8	67·9	98·2	**216·4**	182·2	114·9

[1]Labourers from Tabora diagnosed at Arusha and Moshi Hospitals *People resettled. †New land cleared. ‡Discriminative bush clearing.

Figures in heavy type indicate maximum number of cases. Figures in italics indicate minimum number of cases.

JACKSON, C. H. N. (1944) *Ann. Eugenics*, v. 12, 176. [*Trop. Dis. Bull.*, 1945, v. 42, 186.]
KINGHORN, A., YORKE, W. & LLOYD, L. (1913) *Ann. Trop. Med. & Parasit.*, v. 7, 183. [*Trop. Dis. Bull.*, 1913, v. 2, 235.]
KLEINE, F. K. (1909) *Deut. med. Woch.*, May 27, 924. [*Sleeping Sickness Bulletin*, 1909, v. 1, 249.]
LAMBORN, W. A. & HOWAT, C. H. (1936) *Brit. Med. J.*, June 6, 1153. [*Trop. Dis. Bull.*, 1936, v. 33, 654.]
LLOYD, L. (1930) *Trans. Roy. Soc. Trop. Med. & Hyg.*, v. 23, 533. [*Trop. Dis., Bull.* 1930, v. 27, 846.]
MACKICHAN, I. W. (1944) *Ibid.*, v. 38, 49. [*Trop. Dis. Bull.*, 1945, v. 42, 13.]
MACLEAN, G. (1926) *Ann. Trop. Med. & Parasit.*, v. 20, 329. [*Trop. Dis. Bull.*, 1927, v. 24, 563.]
——. (1927) *Tanganyika Territory Ann. Med. & San. Rep. for 1926*, 85. [*Trop. Dis. Bull.*, 1927, v. 24, 954.]
——. (1928) *Tanganyika Territory Ann. Med. & San. Rep. for 1927*, 129. [*Trop. Dis. Bull.*, 1929, v. 26, 695.]
——. (1929a) *Tanganyika Territory Ann. Med. & San. Rep. for 1928*, 170. [*Trop. Dis. Bull.*, 1930, v. 27, 809.]
——. (1929b) *Ann. Trop. Med. & Parasit.*, v. 23, 37. [*Trop. Dis. Bull.* 1929, v. 26, 696.]
——. (1930) *Tanganyika Territory Ann. Med. & San. Rep. for 1929*, 132. [*Trop. Dis. Bull.*, 1931, v. 28, 342.]
—— & FAIRBAIRN, H. (1932) *Ann. Trop. Med. & Parasit.*, v. 26, 157. [*Trop. Dis. Bull.*, 1933, v. 30, 108.]
POTTS, W. H. (1937) *Bull. Entom. Res.*, v. 28, 129. [*Trop. Dis. Bull.*, 1937, v. 34, 538.]
SWYNNERTON, C. F. M. (1923) *Ibid.*, v. 13, 317. [*Trop. Dis. Bull.*, 1923, v. 20, 311.]
TANGANYIKA TERRITORY, DEPARTMENT OF LANDS & MINES, SURVEY DIVISION (1942) Atlas of the Tanganyika Territory. [*Trop. Dis. Bull.*, 1946, v. 43, 79.]
TAUTE, M. & HUBER, F. (1919) *Arch. f. Schiffs- u. Trop.-Hyg.*, v. 23, 211. [*Trop. Dis. Bull.*, 1920, v. 15, 35.]
TAYLOR, A. W. (1932) *Parasitology*, v. 24, 401. [*Trop. Dis. Bull.*, 1933, v. 30, 105.]

SUMMARY OF RECENT ABSTRACTS *

I. CHOLERA

Epidemiology: Aetiology

STOWMAN (p. 208) has written an account of the world cholera situation in the summer of 1946; in China at least 16 provinces were affected, and Thailand and parts of India had a bad year. The same author (p. 421) makes the point that the 1946 epidemic of cholera in China was one of the most extensive ever recorded in the Far East. He thinks that there are two completely distinct main foci, in the Yangtze and Kwangtung areas respectively; the type of disease seen in the former is more amenable to treatment than that seen in Kwangtung.

PETERSON (p. 1065) shows that the risk of infection in an outbreak in China was about 36 times as great in household contacts as in the general population, and about 5 times as great in unvaccinated as in vaccinated contacts. The information on which these figures are calculated is admittedly so likely to be erroneous that he claims only that the figures are rough indications.

He (p. 1065) found in China that the average period required for stools to become negative for *V. cholerae* was $5{\cdot}4 \pm 2{\cdot}3$ days from the onset of symptoms. In no case were stools positive beyond the 17th day.

PANJA and GHOSH (p. 998) found true *V. cholerae* in 16 of 524 samples of water from the river Hooghly; they used the candle-boric-peptone-water method.

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* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1947, v. 44. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

GALLUT (p. 421) contends that the true cholera vibrio is not Voges-Proskauer negative, as it is usually held to be, but that it can produce acetylmethylcarbinol in sensitive media. It produces considerably less, however, than the El Tor and the Celebes vibrios, and this fact can be used (as well as the haemolysis test) as a basis for differentiation. In a highly technical paper, the same author (p. 660) discusses the oxidation-reduction potential of the cholera vibrio under various conditions of cultivation. The original paper should be consulted for details.

SEN and his colleagues (p. 209) discuss, in two articles, the biochemistry of the cholera-red reaction; these papers cannot satisfactorily be summarized, and should be read in the original.

BRUNEAU (p. 660) has isolated a non-agglutinable vibrio from a patient with typical (but not fatal) cholera in Tonking.

Pathology: Treatment

CHATTERJEE (p. 998) has continued his studies of the bone marrow in fatal cases of cholera, and shows that the characteristic finding is the very great dilatation of the capillaries and sinusoids, which was most remarkable in the bone marrow, but which was also found in many organs. This dilatation, it is suggested, may partially explain the collapse which is a feature of cholera.

In the report of the Scientific Advisory Board of the Indian Research Fund Association for 1946 (p. 998) there is a statement of the results of trials of treatment with various sulphonamides. There is little to choose between the results with sulphaguanidine, sulphasuxidine, sulphadiazine and controls given a placebo, so far as case-mortality is concerned. CHU, HUANG and their colleagues (p. 423) have used sulphaguanidine and sulphadiazine in the treatment of a small number of patients with cholera, in addition to intravenous salines. The results indicate that the average duration of diarrhoea was reduced, but there was no remarkable effect on the time of disappearance of vibrios from the stools. The effects of the two sulphonamides were about equal.

REIMANN *et al.* (p. 423) in China treated a few patients with streptomycin, but do not report any striking favourable results. They think that the important clinical feature of cholera is not intoxication, but dehydration; and that correction of the latter is the chief therapeutic need. If treated properly in this way, cholera becomes much less fatal, with a case-mortality rate of only 5 per cent. Streptomycin and the sulphonamides showed no significant effect in reducing the duration of the carrier state in convalescence. The authors think that cholera is not only water-borne, but is also transmitted directly from case to case; the latter mode of spread was more important than the former, in the outbreaks they describe.

PETERSON (p. 1065) has attempted to evaluate the value of sulphadiazine prophylaxis of cholera in China, but the number of cases which occurred in the trial and control groups was so small that no final conclusions were possible.

Vaccination: Control

BURROWS *et al.* (p. 422), in their introduction to a study of immunity to cholera, comment on the fact that there is little positive evidence on the subject of the efficacy of vaccines; but they conclude that the immunity produced may be in some small degree effective, though leaving much to be desired. The cholera vibrio in its infection remains within the lumen of the gut, that is, virtually outside the tissues of the body throughout the disease. The same authors (p. 422) have investigated the structure of the O antigen of the cholera vibrio, and describe three effective components, A, B and C. A is group-specific; B and C are type-specific for Inaba and Ogawa strains. The possible

types are, therefore, A, AB, AC and ABC ; the last is the Hikojima intermediate type. The authors propose nomenclature according to these letters, instead of the old names ; they note that the O group I of Gardner and Venkatraman contains group-specific antigen A, and that there is no immunological distinction between cholera vibrios and El Tor vibrios of O group I.

In the Report of the Scientific Advisory Board of the Indian Research Fund for 1946 (p. 998) it is stated that of 320 strains of *V. cholerae* isolated, 88·1 per cent. were of Ogawa type, and 11·9 per cent. Inaba.

PANJA and DAS (p. 999) have made a preliminary study of the intradermal inoculation of cholera vaccine in man, and report encouraging results.

WOODWARD (p. 79) reports that a number of men in the U.S. Navy developed symptoms suggesting appendicitis after, and apparently owing to, injection of cholera vaccine.

SEAL (p. 208) notes that in part of Bengal there were 27 outbreaks of cholera within one year. He describes the detailed instructions given to patients and attendants, in relation to treatment (with sulphaguanidine) and prevention. Bleaching powder solution is used for domestic sterilization of discharges, and of the hands ; water and milk should be boiled and food should not be eaten raw. Details should be sought in the original. *Charles Wilcocks*

RABIES

VEERARAGHAVAN, N. **Cultivation of Rabies Virus *in vitro*.** [Correspondence.] *Nature*. 1947, June 7, 782.

The author has previously reported [this *Bulletin*, 1947, v. 44, 635] that the rabies virus will grow in a cell-free medium containing steamed sheep-brains extract, sheep serum, glycine and peptone. The addition of tryptophane (2 mgm. per cc.) stimulated the growth to 25 million MLD in place of 10 million MLD per cc. The addition of biotin, thiamin hydrochloride, pyridoxine hydrochloride, calcium pantothenate, nicotinic acid and riboflavin gave concentrations of 100 million to 50 million MLD per cc. By adding all these substances it was possible to dispense with the sheep-brain extract in the medium. With a medium containing 2·5 per cent. glycine, 2 per cent. sheep serum, 0·15 per cent. peptone, 2 mgm. per cent. tryptophane, 2 μgm. per cc. each of thiamin hydrochloride, pyridoxine hydrochloride, calcium pantothenate, nicotinic acid and riboflavin, together with 0·2 cc. per 100 cc. of biotin solution, concentrations of 5,000 million MLD per cc. were obtained. The virus was also cultivated in a cell-free medium containing 5 per cent. glycine, 0·3 per cent. peptone and 4 per cent. sheep serum. The successful cultivation of the aetiological agent of rabies in the cell-free medium indicated that it is not a virus in the ordinary meaning of the term. [See also this *Bulletin*, 1946, v. 43, 194 ; 1947, v. 44, 634.] *C. M. Wenyon*

AUBRY, G., LAFFARGUE, P. & PORTIER, A. Deux cas d'accidents nerveux de la vaccination antirabique. [**Two Cases of Neuroparalytic Accident after Anti-Rabies Vaccination.**] *Algérie Méd.* 1947, Feb., No. 2, 169–72, 173–4, 175.

The author describes two cases of neuroparalytic accident occurring after anti-rabies inoculation ; it was possible to show that one of these was first caused by the rabies virus. The method employed was the classical one of giving daily inoculations of suspensions of rabbit cords of increasing virulence. The

first patient was a female, aged 35 years. After the fourth inoculation fever, rigors and insomnia appeared, but treatment was continued up to the 8th injection. Twelve days after treatment paralysis appeared in the legs and spread to the arms. Paraesthesia and paralysis of sphincters were also present. Recovery then set in, and was complete without sequelae after one month. The second was a male, aged 53 years. After the 13th injection paraesthesia appeared, with paresis of the legs and difficulty of micturition, followed by paralysis of the arms and right side of the face. Death occurred on the 4th day of illness. On histological examination of the brain, no Negri bodies could be found. A brain emulsion was also inoculated into rabbits, guineapigs and a monkey, but no virus could be isolated. *D. J. Bauer*

MALARIA

FAIRLEY, N. H. **Sidelights on Malaria in Man obtained by Subinoculation Experiments.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, May, v. 40, No. 5, 621–76, 13 charts. [21 refs.]

This important paper deals with the value of subinoculation, as carried out by the Medical Research Unit, A.I.F., in Cairns, Australia, in determining the biological activity and distribution of malaria plasmodia in man, the stage in the life-cycle of the parasite on which anti-malaria drugs act, and the evidence of the existence of an exo-erythrocytic cycle of human malaria parasites. Subinoculation consists in the transfer of whole blood from a volunteer exposed to malaria infection to a volunteer who had never been so exposed. Large quantities of blood were used, 300 to 500 cc. : in one case 800 cc. were transfused. The Julian Smith rotary pump direct transfusion apparatus was used : no anti-coagulant was added to the blood.

Viable sporozoites were demonstrated in the circulating blood for from half to one hour after the inoculation of parasites by anopheline mosquitoes. This is followed by a prepatent period during which pre-erythrocytic forms are presumably undergoing schizogony in reticulo-endothelial cells ; this period lasts six days in *P. falciparum* and eight days in *P. vivax* infections, during which time massive subinoculations of blood from heavily infected individuals persistently fail to induce malaria in recipients. The initial stage of parasitaemia is generally of submicroscopic density : the presence of first generation merozoites is shown by positive subinoculations, and it is generally about three days before parasites are demonstrated microscopically. Minor premonitory clinical symptoms may be present during this initial stage of parasitaemia. There is a characteristic left polymorphonuclear shift, a relative leucopenia and a decrease in lymphocytes.

In *P. falciparum* malaria, parasites are first seen in films 9·5 days after a single exposure to infection (range 7 to 12 days). Trophozoite densities increase in phase rapidly ; a big rise each 48 hours is followed by a smaller fall. In untreated heavy infections, clinical evidence of hyperinfection is manifest about the 17th or 18th day ; from the 21st day, 20 per cent. or more of the red cells may be infected. In *vivax* malaria parasites are first found in thick films about 12 days after infection (10 to 17 days). Trophozoite densities increase only gradually, the curve being sigmoid in form : the mean density in untreated cases was 8,270 per cmm. by the 20th day.

The clinical attack is followed by a latent phase. In uncured *falciparum* infections in this phase, subinoculations are positive though it may be impossible

to find parasites in films. A negative subinoculation indicates radical cure. In *vivax* infections, subinoculations may be repeatedly negative yet malaria attacks may occur later.

In *falciparum* infections, asexual parasites persist in the blood, maybe in submicroscopic densities, throughout the period between recrudescences. In *vivax* infections, the blood is frequently cleared of parasites in the intervals between recrudescences, relapses and recurrences. Apparently exo-erythrocytic forms persist in *P. vivax* infections; in *P. falciparum* infections, they are presumably converted entirely into first generation merozoites.

Subinoculation experiments in volunteers taking adequate daily doses of anti-malaria drugs and failing to develop overt malaria gave information regarding the mode of action of these drugs as suppressants or causal prophylactics. They showed that paludrine and plasmoquine are complete causal prophylactics of *P. falciparum*, but only partial causal prophylactics of *P. vivax*.

When schizonticidal drugs of the atebrin type are given in adequate doses each day for suppressive purposes, positive subinoculations are obtained with 200 cc. blood on the 7th day after infection with *P. falciparum* and on the 9th day with *P. vivax*, just as if no drug were administered. Though parasites are not found in blood smears, they can be demonstrated by subinoculation for the next 3 to 5 days, but not subsequently.

Trophozoite-induced *vivax* malaria was radically cured by atebrin in suppressive or therapeutic dosage, but radical cure of sporozoite-induced *vivax* malaria was difficult to attain. Not more than 18 per cent. of volunteers receiving one course of Q.A.P. treatment for *vivax* malaria were radically cured. This different therapeutic response appears to be due to the persistence of late exo-erythrocytic forms which are resistant to treatment and which, after a variable time, liberate micromerozoites into the blood stream. There is no evidence that asexual parasites give rise to late exo-erythrocytic forms in *vivax* infections.

Norman White

SHUTE, P. G. **Indigenous Malaria in Great Britain.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1947, July, v. 6, 116–21, 2 charts.

This note by the Assistant Malariologist, Ministry of Health, gives a brief account of the incidence of malaria as caused by the four recognized species of parasite, and of the means whereby it may be spread. It is noted that *P. vivax* is the only species likely to constitute a public health problem in England. The number of cases of *P. vivax* malaria reported in England between 1917 and 1946 is shown in a table, from which it is noted that there were 235 cases in 1917, 35 in 1920, and from 1 to 6 cases each year between 1922 and 1943. There were 9 cases in 1944, 8 in 1945, and 6 in 1946. Most of those cases occurring in recent years were traceable to servicemen who had relapsed; and the infections could usually be associated with the proximity of *Anopheles maculipennis*.

This is the only species of mosquito which has been proved to be concerned in the spread of malaria in Britain. *A. maculipennis* is seldom found inside large towns, and indigenous malaria occurring in town dwellers in Britain is almost certainly contracted in rural areas. This was evidenced in the case of recent notifications of malaria in London children [this *Bulletin*, 1947, v. 44, 789, 790] who had contracted the disease elsewhere.

The author discusses the complexity of the problem of the insect vector and the potential hazards arising from the presence in Britain of relapsing cases of *P. vivax* malaria. Finally, a timely reminder is given that indigenous malaria is a notifiable disease and that blood films are examined free of charge at the Ministry's Malaria Laboratory, Horton. *H. J. O'D. Burke-Gaffney*

NASCIMBENE, A. & PREZIOSO, A. La lotta antimalarica in provincia di Pavia (studio riassuntivo degli anni 1932–1945). [**Antimalaria Campaign in the Province of Pavia.**] *Riv. Ital. d'Igiene.* 1947, May–June, v. 7, Nos. 5/6, 192–212, 1 map & 2 charts. English summary (6 lines)

This is a description of the Province of Pavia, from a malaria standpoint, and of the activities of the Provincial Antimalaria Committee. There has been very little endemic malaria in recent years. In 1932, there were 144 notified cases in 31 communes; in 1945 there were but 4 cases in 3 communes. In addition, there were numerous imported cases at the time of the Abyssinian war and during the world war. Very little has been done in the matter of anopheline control. Nearly all infections are due to *P. vivax.*

Norman White

MATHIEU, M. Le paludisme dans l'Atacora. Circonscription médicale de Natitingou-Dahomey. [**Malaria in Atacora District (Dahomey).**] *Bull. Méd. de l'Afrique Occidentale Française.* 1946, v. 3, No. 2, 267–9.

Three different tribes occupy the Atacora Circle which occupies an area of 22,000 square kilometres and possesses a total population of 148,000. The author was struck by the infrequency of mosquitoes there and, therefore. examined the degree of malarial endemicity in the region.

Figures of attendances at medical institutions from 1936 to 1945 indicated that the number of cases of malaria notified varied between 3 and 8 per cent. of all patients seen (from 9,214 persons examined in 1936 to 21,090 in 1945).

These figures are, however, only applicable to urban centres: the author therefore consulted the records of the local sector of the Mobile Hygiene Service, which indicated that the percentages of blood films found positive for malaria for 1943 to 1945 were respectively 50·12 (28,648 blood examinations); 51·87 (28,288); and 73·90 (55,046): the most recent parasite rate was therefore about 74 per cent.

Clinical malaria in children was frequent and serious and was caused entirely by *P. falciparum.* Splenic indices from children aged 2 to 12 years in three schools are given as 23·78, 14·31, and 11·17 per cent. [but it is noted that only 185, 35 and 170 children were examined].

The gametocyte rate varied between 12 and 14 per cent. The author fixed the "Ross index" at 50 [it is not stated whether the endemic index of Ross or the "index of Ross" of Brumpt is implied].

The author concludes that Atacora should be considered as an area of high endemicity and points to the danger inherent in the casual attitude of the inhabitants to malaria because of the comparative rarity of mosquitoes [the mosquito vectors are not mentioned].

H. J. O'D. Burke-Gaffney

HAIRSTON, N. G., BANG, F. B. & MAIER, J. **Malaria in the Natives of New Guinea.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 795–807, 5 figs. & 1 map.

An examination of spleens and blood smears was carried out in nine different areas of New Guinea: the results are tabulated. Over 2,000 natives were examined. Malaria was found to be hyperendemic in all areas, but there was considerable variation in the intensity of transmission. In one village, malaria was so intense that the incidence of palpable spleen was highest in the 0–2 age group: older children had sufficient immunity to determine a lower spleen rate. The spleen rate of children in this village was 68 per cent., but it had

more malaria than had another village with a children's spleen rate of 94 per cent. These observations indicate the importance of classifying results according to age groups.

The authors consider the plasmodimetric index, measuring the parasite load of the population [see this *Bulletin*, 1943, v. 40, 739] to be a useful adjunct to the standard survey; the positive blood smears are divided into categories according to the number of parasites found per 500 white blood corpuscles.

Norman White

PAUL, J. H. & BELLERIVE, A. **A Malaria Reconnaissance of the Republic of Haiti.** *J. National Malaria Soc.* 1947, Mar., v. 6, No. 1, 41–67, 4 figs. [13 refs.]

The Republic of Haiti occupies the western third of the second largest island of the West Indies; the remaining two-thirds constitute the Dominican Republic. The Gulf of Gonave almost bisects Haiti into two peninsulas. The country is mountainous. There is only one river of any size, the Artibonite. Most of the other streams are intermittent; nearly all are blocked at the mouth by sand or gravel bars; the resulting lagoons are productive of anophelines. The principal human settlements are on the coast near such streams.

The population of the Republic is almost entirely Negro. The few whites and Asiatics are confined to the more important commercial centres. The population is about two millions. Port-au-Prince, the capital, has between 100,000 and 200,000 inhabitants; there are no other large cities. The economy of Haiti is purely agricultural. No reliable vital statistics are available.

In 1940, arrangements were made between the National Health Service and the Rockefeller Foundation to carry out a malaria survey of the whole republic. The field work was limited to an examination of schoolchildren. All schoolchildren were examined for splenomegaly. The blood of all children with enlarged spleens and of 25 per cent. of children with normal spleens was examined. In villages with less than 50 schoolchildren, all were examined for parasites. In all 31,285 children in 826 primary schools were examined. The spleen rate of children in schools at altitudes of less than 1,000 feet was 29·8; between 1,000 and 2,000 feet 13·5, over 2,000 feet 6·2 per cent. The highest spleen rate (20·6) and the largest average spleen were found in the youngest age group, 0-4. The higher the splenic index of an area, the higher was the incidence of parasitaemia both in those with normal spleens and in those with splenomegaly. For the country as a whole, children with normal spleens had a parasite rate of 21 per cent.; the group with the smallest amount of splenic enlargement, palpable on deep inspiration, had a parasite rate of 68; parasite rates of 78, 80, 80 and 100 per cent. were found in children with ascending sizes of spleen. Of all infections, 86·6 per cent. were *P. falciparum*, 8·9 per cent. *P. malariae* and only 1·9 per cent. *P. vivax*. Only 2·6 per cent. were mixed infections; slides were not ordinarily studied for more than five minutes. Triple infections were noted nine times.

Three species of anophelines were found: *A. albimanus*, *A. grabhami* and *A. vestitipennis*. *A. albimanus* was ubiquitous. It had a wide variety of breeding places, but preferred a sunlit situation. *A. vestitipennis* was found breeding only in one shaded swamp. *A. grabhami* was found in 19 of the 27 arrondissements, breeding with *A. albimanus* or alone in streams or canals that were heavily shaded. Numerous dangerous breeding areas are man-made.

The clinical manifestations of malaria rarely arrest attention except among the infants of the community. The few areas of Haiti that are malaria-free are the higher mountain valleys and the south-west slopes where the rainfall is very low.

Norman White

NIETO CAICEDO, M. Epidemia regional de malaria en la cuenca del Lago de Maracaibo 1942–1943. [**A Regional Epidemic of Malaria in the Basin of Lake Maracaibo, Venezuela, in 1942-1943.**] *XII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora. No. 23.* Caracas. 1946, June, 288+xx pp., 32 figs. on 21 pls., 8 maps (3 folding) & 43 graphs (10 folding). [25 refs.] English summary.

This study, of close on 300 pages, discusses in very considerable detail, and with a wealth of tables, charts, diagrams and other illustrations, a wide regional epidemic of malaria which occurred in Venezuela in 1942–43 and the measures applied against it.

The area concerned was the basin of the Maracaibo Lake in Zulia State.

Topographical and meteorological data are fully discussed: the level of the lake is inconstant and flooding into surrounding country leads to the formation of breeding places for mosquitoes. The local temperature averages about 82°F., the humidity ranges from 70 to 85 per cent., and the rainfall varies greatly: an unusually heavy rainfall during 1942 preceded and contributed to the epidemic.

Sociological features are described and the incidence of malarial morbidity and mortality is discussed at length. The local distribution of anophelines is shown, and it is noted that *A. albimanus* is more prevalent in the northern desert-like regions and *A. darlingi* in the southern jungle. It is stated that previous epidemics of malaria have shown some "para-quinquennial periodicity".

Full figures are given for the prevalence of anophelines in breeding places and dwelling houses in the city of Maracaibo: the oöcyst-rate was 5 per cent. The epidemic lasted from November until March, with a peak in January: during that period, 17,201 cases were actually recorded; but it was estimated finally that the total was in the neighbourhood of 40,000.

In 7,989 blood films examined, an infection rate of 50·4 per cent. was found. In the town of Maracaibo, *P. vivax* prevailed, but *P. falciparum* was prevalent in 40 per cent. of the rural outbreaks seen.

The general mortality for Zulia State as a whole "surpassed in 406 deaths the expected mortality according to the median: and the mortality from both malaria and 'fever' together exceeded by 473 the corresponding median."

The control measures adopted included free distribution of 50,000 complete quinine treatments and the usual methods of controlling *Anopheles* larvae and adults.

[This study represents a very fully documented account of an extremely large epidemic.]

H. J. O'D. Burke-Gaffney

ANGELINI, G. Incertezza dei reperti di "forme esoeritrocitiche" dei plasmodi della malaria umana nel midollo osseo. [**Unreliability of Reports of Exoerythrocytic Forms of Parasites of Human Malaria in the Bone Marrow.**] *Riv. di Parassit.* Rome. 1947, Mar., v. 8, No. 1, 5–18. [Refs. in footnotes.] English summary (7 lines).

The author examines the various records which have been made of the occurrence in smears of the bone marrow and other organs and in sections of tissues of exoerythrocytic schizonts of human malarial parasites. He finds that detached portions of the cytoplasm of cells may simulate these stages, as occurs commonly in smears of bone marrow, and comes to the conclusion that up to the present no reliable morphological record of these stages in human malaria has been made. The paper is a useful one in that it reviews the various papers which have been published on this subject.

C. M. Wenyon

BLACK, R. H. **The Consumption of Haemoglobin by Malaria Parasites.** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 215–17, 8 coloured figs. on 1 pl.

Hitherto, evidence of the consumption of haemoglobin by malaria parasites has been derived from studies of (1) the pallor of infected red cells, (2) the formation of malarial pigment and its identification with haematin, and (3) respiration of plasmodia in monkeys.

The present author bases his study on the staining reaction of cyanol with haemoglobin in thin blood films containing malaria parasites, obtained from human and animal sources.

Cyanol (colour-index 715) in the reduced and colourless state, is oxidized in the presence of haemoglobin, which it stains blue. The author applied to blood films the method of staining haemoglobin in sections described by DUNN [this *Bulletin*, 1946, v. 43, 1081] ; this resulted in the washing out from red cells of the blue-stained haemoglobin, as Dunn's working reagent was found to be too acid for films.

The following procedure was therefore evolved :—

Dunn's stock solution is prepared by dissolving 1 gm. of cyanol in 100 cc. of distilled water and adding 10 gm. of zinc powder (C.P.) and 2 cc. of glacial acetic acid ; the mixture is boiled and quickly loses its blue colour.

The working stain is prepared immediately before use and consists of 5 cc. of filtered stock solution (which has been kept over the zinc) and 0·5 cc. of 3 per cent. hydrogen peroxide.

As a counterstain, either 1 per cent. aqueous safranin or diluted Leishman's stain was used. The different species of plasmodia showed distinctive staining with safranin, *e.g.*, *P. gallinaceum* stains pink, while *P. vivax* is much lighter in colour. With Leishman's stain, there is no eosinophilic staining of the red cell, which remains cobalt green.

With the above methods, normal red cells stain cobalt green : parasites stain variously, *e.g.*, pink (with safranin in *P. gallinaceum* infections), a faint-brownish yellow (with safranin and *P. vivax*), or blue-red (with Leishman's stain in *P. vivax* and *P. falciparum* infections). Safranin stains nuclei of fowl red cells a warm yellow-brown ; malarial pigment, although prominent, apparently does not react with cyanol under the conditions described.

Young forms of parasites did not show any apparent loss of cyanol-staining material in the containing red cells ; large rings showed a loss of green colour from their immediate neighbourhood. With amoeboid forms, the containing red cell showed only a little green colouration ; the remaining green was distributed irregularly through the cell and was seen in the area not immediately in contact with the parasite. In *P. gallinaceum* infections, where there is little amoeboid activity, the green stain was absent only from the part of the cell occupied by the parasite.

Little, if any, staining with cyanol was shown by red cells containing fully grown parasites, such as *P. vivax* or *P. falciparum* gametocytes and *P. knowlesi* schizonts.

[All these forms are clearly shown in eight figures on a coloured plate.]

The usual appearances described in relation to infected red cells stained by the common methods are discussed, together with past views on the reduction colour in red cells infected with malarial parasites. The author concludes, from the experiments described, that the actively amoeboid and more slowly growing parasites use the haemoglobin from most of the red cells, while the relatively inactive species merely use that in their immediate neighbourhood.

H. J. O'D. Burke-Gaffney

MacDougall, Mary S. **Cytological Studies of *Plasmodium*: the Male Gamete.** *J. National Malaria Soc.* 1947, June, v. 6, No. 2, 91–8, 18 figs. on 5 pls. [37 refs.]

The study of the production of male gametes of *P. vivax* and *P. falciparum* has shown the author that chromosomes appear in the process. The films were wet fixed and stained by Giemsa or haematoxylin. The earliest stage is that of four granular bands which are followed by four pairs of chromosomes arranged in a row. Next there occur two parallel bands which can be described as the pachytene stage. At this stage, the male gametes begin to form and four pairs of chromosomes are differentiated from the pachytene stage. Only one paired mass of chromatin enters each male gamete but each may represent more than one pair of chromosomes. When fertilization occurs, the male gamete with its pair of chromosomes enters the female gamete. In some cases, sterile male gametes are formed without any chromatin and it seems that in certain strains of parasite these sterile males preponderate. In such cases mosquito infection is difficult. There are many gaps in the cycle and further studies are in progress. The paper is illustrated by a series of micro-photographs and line drawings.

C. M. Wenyon

Basu, B. C. **Abnormal Development of Malarial Oöcysts in *Anopheles stephensi*.** *Indian J. Malariology.* 1947, Mar., v. 1, No. 1, 129–32, 3 pls.

Three abnormalities were noticed in malarial oöcysts in the gut of artificially infected *Anopheles stephensi*. The "black spores" of Ross were found in 2 of 173, 13 of 354 and 4 of 61 mosquitoes fed on *P. vivax*, *falciparum*, and *malariae* carriers respectively. In *falciparum* infections, oöcysts were occasionally found in the lumen of the gut, instead of in the outer layer, and it is concluded that such mosquitoes would not become infective. The third abnormality was seen in a *vivax* case where "twin" oöcysts occurred, probably as the result of two zygotes settling down close together.

P. C. C. Garnham

Peus, F. Die Stechmücken und ihre Bekämpfung. Teil I. Die Fiebermücken des Mittelmeergebietes. [**Mosquitoes and their Control. Part I.** *Anopheles* **of the Mediterranean Region.**] *Hyg. Zool.* Leipzig. 1942, v. 8, 150 pp., 170 figs. & 2 folding keys. [15 refs.]

The author has produced a general summary about the *Anopheles* of the Mediterranean region which is, at least in most respects, accurate and well illustrated. It would be suitable for a man who was to practise hygiene in that area, assuming that he had a slight general knowledge of entomology.

The introduction, which runs to about sixty pages, gives the characters of the genus *Anopheles* and the external anatomy of these insects with special reference to points used in determining species. The larger and more special part of the work deals with the Mediterranean species. The geographical limits of the region are defined in such a way as to exclude Persia, which is perhaps unfortunate. The author then gives a list of the species known to occur in the region, with lists of those found in the separate countries. This is followed by an account (generally two or three pages with text figures) of each species, with its diagnostic characters, geographical distribution, biology and importance in relation to malaria. The total number of species in the region is given as twenty, counting *A. maculipennis* as one: but the author points out that many of these are found only in a very limited part of the region, but that eight are of fairly wide distribution within it. One observes a few points on which the expert would disagree with the author: for instance it is

stated that *A. superpictus* occurs in Spain and Portugal, which is probably an ancient error based on a misidentification. The work is concluded with keys to the adult and last larval stage, and with a list of principal books and monographs, which does not seem to have been very well selected. *P. A. Buxton*

AMARAL, A. D. F. & PENIDO, H. M. Distribuição dos anofelinos no Vale do Rio Doce (Percurso da E. F. Vitória a Minas). Espécies Transmissoras da Malária. [**Distribution of Anophelines in the Neighbourhood of the Rio Doce.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1947, v. 1, No. 1, 163–78, 1 map. English summary.

Studies of species of anophelines were made along a part of the Vitoria-Minas railway, which runs from Vitoria on the coast of the State of Espirito Santo to Presidente Vargas in Minas Gerais.

During 1943, 544,938 anopheline larvae and 10,973 adults were captured in human dwellings: an additional 1,022 adults were captured out of doors. Dissections of 1,118 stomachs and salivary glands indicated that *Anopheles darlingi* and *A. albitarsis* were naturally infected and were the vectors of malaria in that area. Infections were found in the stomachs of 7·5 per cent. of 781 *A. darlingi* examined and 1·3 per cent. of 226 *A. albitarsis*.

In 7,094 blood films examined, malaria parasites were found in about 5 per cent. *P. falciparum* accounted for about one-half of these.

Details of these figures and of species distributions are shown in seven tables. *H. J. O'D. Burke-Gaffney*

WEXLER, L., ADAMS, H. V. & GOLDBERG, L. C. **The Accidental Appearance of Quartan Malaria in a Therapeutic Malaria Treatment Center.** *Amer. J. Syph.* 1947, Sept., v. 31, No. 5, 518–21, 2 figs.

Quartan malaria is rare in the United States. The authors record the case of a Negro soldier, aged 36, admitted to a hospital in Augusta, Ga., for treatment of neuro- and cardiovascular syphilis. Fourteen days after admission, the patient complained of backache, joint pains and myalgia. His temperature exceeded 102°F. that evening, fell to normal next morning and rose to 101°F. in the afternoon. A blood smear was negative. For several days, a quotidian type of hyperpyrexia continued. On the 10th day of the fever (during which daily blood examinations had been made) quartan malaria parasites were found in the patient's blood. The malaria was terminated by treatment with chloroquine (S.N. 7618).

The origin of the infection is discussed. The patient was born in Alabama, and except for yearly visits to Panama City, Florida, between 1931–1940, had not left there until he entered the army in 1944. Thereafter, he served in Wyoming and Massachusetts and later in Europe (England, northern France, Luxembourg and Germany) until November 1945. On returning to the United States, he lived for some weeks in Arizona and thereafter in his birthplace, Birmingham, Alabama. Nothing in his history could be attributed to malaria, and he had never had any blood transfusions. The hospital ward to which he was admitted was a therapeutic malaria ward, where quartan and tertian strains were used: it was well screened and sprayed each month with residual DDT.

As the patient had been receiving bismuth injections, the possibility of syringe or needle transmission was considered and abandoned, though it is added that frequent use and exchange of syringes and needles takes place, because of routine penicillin therapy; however, sterile technique was always used.

Malaria is widespread in the south-eastern States, but the quartan parasite has "an unexplained spotty distribution". A delayed onset or a relapse of a

previous autochthonous infection was not found to be wholly compatible with the patient's history; the final possibility is therefore considered that transmission was by an anopheline from a patient receiving therapeutic quartan malaria. Inspection proved the presence of *Anopheles quadrimaculatus*, *A. punctipennis* and *A. crucians* less than 850 yards from the hospital. It is stated that the incubation period of mosquito-induced quartan malaria "varies from thirty to forty-nine days, yet exceptions may prove the rule, as in this reported case."

The authors re-emphasize the need for screening wards inhabited by patients receiving therapeutic malaria, and for providing mosquito nets where anopheline vectors are known to occur locally, a conclusion already drawn by MAYNE and YOUNG (*Venereal Dis. Information*, 1941, v. 22, 271). Strict asepsis is essential in such wards, "since the possibility that this reported infection might have been introduced through syringe or needle cannot be completely dismissed."

H. J. O'D. Burke-Gaffney

HÖRING, R. O. **Induced and War Malaria.** *J. Trop. Med. & Hyg.* 1947, Aug., v. 50, No. 8, 150–59, 6 figs.

This paper records the experience of a bridge-construction party of the German army, 214 strong, none of whom had been previously exposed to malaria. In the summer of 1941, they were near Larissa in Greece; 116 contracted malaria—112 *P. vivax* infections, 2 *P. falciparum* and 2 mixed. Ninety-six of the benign tertian cases were followed up; 74 relapsed. The total number of relapses was 159. The author compares the results of his observations with the 161 cases of induced *P. vivax* malaria reported by JAMES and NICOL in 1932 [quoted from *Discussion*, reviewed in this *Bulletin*, 1933, v. 30, 76]. The similarities are striking and confirm James's opinion that there are no great differences between induced and naturally acquired infections. The relapse rate was, however, much higher in the author's cases than in those reported by James. The author believes that tendency to relapse is associated with the massiveness of infection. A multiplicity of infective anopheline bites may result in infection with heterogeneous strains.

A graph shows the number of patients that suffered 1, 2, 3, 4, 5 or 6 relapses. The decline is in the nature of a simple exponential curve, which would also express the chances of the individuals receiving no, one two, three, or more infective bites.

The cases studied indicated that the longevity of *P. vivax*, once the parasite has entered the body, in its endo- or exo-erythrocytic stages, with or without atebrin treatment, overt or subclinical, lasts one and a-half years and no longer.

Norman White

BIANCO, A. A., SAUNDERS, G. M., LEVINE, A. S. & COHN, R. **Long-Term Observation of *Plasmodium vivax* Malaria in the Returned Serviceman. Parts II & III.** *U.S. Nav. Med. Bull.* 1947, May–June & July–Aug., v. 47, Nos. 3 & 4, 550–67; 753–65, 5 figs. [27 refs.]

There is a general impression that *P. vivax* malaria acquired in the South Pacific has a special tendency to relapse over very long periods. Many patients exhibit such a tendency but many others have suffered only one to four relapses during two years, though the place and degree of exposure to infection were identical with those of the group of chronic relapses who suffered up to 20 proved relapses. The future clinical course of malaria appears to be determined by an unknown clinical factor, or factors. Repeated relapses have also been known in patients who acquired infection in the Caribbean, Mediterranean and China areas.

In patients observed personally in two or more relapses who had been out of endemic malaria areas and off suppressive mepacrine for more than a year, there was a lengthening of the period between relapses. These patients began to tolerate malaria a great deal better; the attack produced only mild discomfort and responded to very small amounts of antimalaria therapy. Spontaneous remission may occur. But occasionally a severe relapse will occur 3 years after exposure to infection; this is, however, very exceptional.

Numerous expedients were tried to precipitate relapses; all failed. They included erythema doses of ultraviolet light; deep X-ray therapy to the spleen; adrenaline subcutaneously; a course of desoxycorticosterone injections; infusion of 1,000 cc. of physiological saline solution via the spleen; diathermy to the spleen for 7 days; immersion in an ice-cold bath to the limit of tolerance; penicillin in maximum dosage; calcium pantothenate, 45 grains daily for 7 days; ketogenic diet with 60 grains of ammonium chloride daily for 7 days; exposure in a pressure chamber, equivalent to 18,000 feet altitude, for five hours; gradually increasing insulin up to 100 units daily, for 14 to 21 days, with periods of hypoglycaemia of 3–4 hours before administration of dextrose; most strenuous exercise.

For treatment, atebrin [mepacrine] is superior to quinine. The officially recommended total dosage, 2·8 gm. in 7 days, is effective and nothing is gained by increasing the dose. Where prompt return to duty is imperative, the "flash" treatment may be useful. The patient receives simultaneously 0·4 gm. atebrin intramuscularly and 0·2 gm. orally, followed by 0·2 gm. orally every 4 hours, for 3 doses, a total of 1·2 gm. in 12 hours. This is followed by 0·1 gm. a day as long as the patient remains in an endemic area, or for 10 to 16 days if on duty in a non-endemic area. This régime compared favourably with the 7-day standard treatment; within 48 hours the patients were ambulatory.

Seventeen patients were treated with plasmoquine-quinine; there was only one relapse during a 120 days' observation period, much the best result obtained with any treatment.

Chronic headache was the most frequent residual symptom which followed treatment of an acute relapse. An extensive electro-encephalographic study was made of these headaches. The qualitative and quantitative electro-encephalogram findings in headaches occurring in chronic recurrent malaria and in headaches unaccompanied by any recognized disease process involving structural changes were almost identical. This indicates that malaria headaches are not an integral part of the malaria infection.

Part III of this paper deals with neuropsychiatric problems in patients suffering from recurrent *vivax* malaria. Psychogenic illness was found to be no different in nature or in frequency in these patients than in a non-malaria group of patients. In each case of mental illness, total personality studies are indicated; malaria is only another incident in the total environment of the personality under study. *Norman White*

MATEO ALONSO, A. Estudios sobre los cuadros clínicos más graves del paludismo. [**Clinical Study of the Severer Forms of Malaria.**] *XII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora. No. 22.* Caracas. 1946, 74 pp., 3 graphs & 9 figs. [Bibliography.]

The first part of this article treats of the cerebral forms of malaria. The author's remarks are based on cases which occurred during an epidemic in 1945. In the latter half of the year, 194 cerebral cases were seen, 152 of them first attacks. One hundred and eighty-seven were children between 6 months and 5 years of age; the other seven were respectively 3 of 6 years and one each of

7, 9, 13 and 20 years. Of the 152 first attacks 84 were in males, 68 in females; 18 died, 11 boys and 7 girls. A more detailed table of cerebral symptoms shows that of the 194 there were 56 with signs of meningitis, 43 with status epilepticus, 32 with fits of an epileptic type, 28 of coma, 19 with fits apoplectic in type, and 16 with "symptomatic epilepsy". General remarks are made on these and four cases are detailed. [Attempts have been made to illustrate them by photographs, but all are out of focus and unrevealing.] The last few pages are devoted to discursive remarks on the possible effect of sunlight in the causation of blackwater fever. *H. Harold Scott*

BONNE, C. Malaria haemorrhagica. [**Haemorrhagic Malaria.**] *Med. Maandblad.* Batavia. 1947, July, No. 12, 223–4.

The English summary appended to the paper is as follows:—

"Description of two typical cases of haemorrhagic malaria with severe haemorrhages from the bowel and in one case epistaxis, in the other case haematemesis. Both patients showed a few purpuric haemorrhages into the skin. Large scale blocking by parasite-containing blood corpuscles of capillaries of the intestinal canal as well as of the brain and other organs was present. There were no signs of complicating diseases."

TEMKINE, M. La pathologie et la thérapie de l'hémoglobinurie paludéenne. [**Pathology and Treatment of Malarial Haemoglobinuria.**] *Rev. Paludisme et Méd. Trop.* 1947, Oct. 15, v. 5, No. 41, 239–41.

MONNEROT-DUMAINE, M. & SANANES, N. La forme suraiguë de l'anémie splénique hémolytique du paludisme. [**Hyperacute Haemolytic Splenic Anaemia in Malaria.**] *Rev. Paludisme et Méd. Trop.* 1947, Oct. 15, v. 5, No. 41, 233–8.

NELSON, M. G. **Serological Tests for Syphilis in treated** *Plasmodium falciparum* **Malaria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Sept., v. 41, No. 1, 127–32.

The author discusses the literature on the false positive serological tests for syphilis which sometimes occur in sera from persons having malaria; these results particularly require recognition in persons suffering concurrently from non-syphilitic venereal disease and malaria, in whom latent syphilis might be suspected.

At the R.A.F. Hospital, Takoradi, Gold Coast, an investigation was made by the author on the sera of 200 Europeans suffering from acute *Plasmodium falciparum* infections: the cases constituted unselected consecutive admissions in all degrees of clinical severity, in whom syphilis was excluded by all possible methods. All patients received full anti-malarial treatment upon diagnosis.

Blood was taken within 24 hours of the finding of the parasites and again on the 10th day after the first paroxysm. The sera were tested in parallel against the Ide, Meinicke and Kahn antigens: positive sera were subjected to the Kahn verification test.

The results of different stages are shown in four tables. False positive results were found in about 3 per cent. of cases, the three tests being in satisfactorily close agreement (Ide 2 per cent., Meinicke 4 per cent., Kahn 3 per cent.). The author refers to the comparable investigation by ELMES and FINDLAY in 80 patients in West Africa [*Bulletin of Hygiene*, 1945, v. 20, 254]: these workers found 23 false positive results with the Kahn and 4 with the Ide test.

The present author found the Ide test a useful slide method which correlates fairly well with the Kahn reaction: he shows in a table the results of 1,000 sera tested in West Africa against the three antigens in parallel: in primary and

treated syphilis, the Meinicke was the most sensitive test and the Ide the least: in the few secondary cases examined, agreement was complete: no non-specific reactions occurred in cases of non-syphilitic venereal disease. The percentages of positive results were, Ide 49, Meinicke 80·4, Kahn 65·4. Discrepant results were found in the sera of 200 healthy Africans examined for evidence of latent yaws or syphilis: the percentages of positive results were, Ide 28, Kahn 37, Meinicke 48·5.

The author considers the Meinicke to be the most sensitive flocculation test under tropical conditions.

False positive results in treated malaria occurred in the first 14 days, and sera were negative, in those followed up, within 40 days of the first paroxysm. The author quotes KITCHEN *et al.* [*Bulletin of Hygiene*, 1939, v. 14, 619], who found most of the false positives between the 15th and 21st days: the results remained positive for 2 months. He also refers to the work of DAWBER [this *Bulletin*, 1944, v. 41, 364]: the optimum time for obtaining false positive results is later in untreated than in treated malaria and the sero-positivity lasts longer.

False positive results due to malaria can be distinguished from true syphilitic reactions by (1) serological follow-up, and (2) verification tests. Since malarial false positives only persist for about 1 month in treated cases and 2 months in untreated ones, follow-up for 2 months after full anti-malarial treatment should allow of a differential diagnosis. The author did not find that either the Kahn verification test or the Richardson potentiation test could be relied upon in the tropics to distinguish true from false positive reactions due to malaria.

The author notes the difficulty of achieving serological specificity in areas where yaws is endemic: in any case, even where syphilis and yaws can be excluded, certain other factors affect the interpretation of false positive results, of which the following are important:—

(1) *P. vivax* gives more false positives than *P. falciparum* [KITCHEN, *loc. cit.*]

(2) The results vary in the different clinical stages of the disease [KITCHEN, DAWBER, *loc. cit.*]

(3) Anti-malarial treatment results in fewer false positives than occur in untreated cases, and these results occur earlier (2 weeks) in treated malaria than in untreated cases (3rd week).

(4) Results on the same sera vary greatly with the test employed: on the whole, the Wassermann reaction is more sensitive to false positive sera in *P. falciparum* malaria and the Kahn test in *P. vivax*.

[For a discussion of false positive tests, see the review of Serum Tests for Syphilis, by T. E. OSMOND, *Bulletin of Hygiene*, 1946, v. 21, 627.]

H. J. O'D. Burke-Gaffney

CHINN, M. Nouvelle enquête sur les séroréactions de Bordet-Wassermann et de Kahn dans la malaria. [**A New Study of Wassermann and Kahn Reactions in Malaria.**] *Ann. Soc. Belge de Méd. Trop.* 1947, Mar. 31, v. 27, No. 1, 5–15.

The author, working in the Medical Laboratory at Coquilhatville, was prompted to make this study as a result of finding strongly positive WR and Kahn reactions in a European during an acute attack of malaria. Syphilis could be excluded clinically and the patient's serological tests had been negative a few weeks earlier.

After discussing British, American and Belgian workers' views on biological false positive reactions in malaria, the author describes tests made by himself on 265 African children, between the ages of 1 and 13, in whom syphilis could

practically be excluded, but who were suffering from acute malaria with parasites in their blood. The first 40 comprised children of under 5 years: only one showed a positive WR and Kahn, and he also showed some evidence of yaws.

The other 225 were chosen from 752 school-children of 5 to 13 years in Coquilhatville and neighbourhood, 70 per cent. of whom were harbouring malaria parasites. All the 225 children tested harboured parasites, commonly *P. falciparum*, sometimes *P. malariae* and rarely *P. vivax*.

There were 16 positive WR and Kahn reactions. Most of the children concerned showed evidence of yaws, and only four could be regarded as non-specific; of these, only one was beyond doubt.

The author then discusses the literature on the subject published in other countries, which he studied in abstracts in this *Bulletin* between 1943 and 1945. The authors studied were in two groups (*a*) German workers, particularly concerned with serological reactions in *P. vivax* infections, and (*b*) American workers, who were concerned with reactions in infections caused by all three species. [The relevant material will be found in this *Bulletin* during the years quoted.]

The present author considers that false positive sero-reactions in the local Africans are due almost entirely to some cause other than malaria. In places where malaria is highly endemic and prophylaxis and treatment are largely absent, it does not provoke false reactions in these people, except in perhaps less than 1 per cent. The author considers that such false positive results are also uncommon in Europeans in the tropics, except when they acquire their first acute attack. Prevention and treatment have made this type of attack increasingly rare. In 86 WR and Kahn tests in Europeans during the current year, the author found six positives, all of which were in accordance with the clinical diagnoses.

Nevertheless, he believes that in exceptional cases, the possibility of malaria as a cause of false positive Wassermann and Kahn tests must be borne in mind, where the serological results conflict with the clinical features [see above].

H. J. O'D. Burke-Gaffney

SAPERO, J. J. **New Concepts in the Treatment of Relapsing Malaria. The Charles Franklin Craig Lecture, 1946.** *Amer. J. Trop. Med.* 1947, May, v. 27, No. 3, 271–83. [19 refs.]

In this address, the author discusses recent conceptions which help to explain the very divergent claims that have been made in the past regarding the efficacy of various therapeutic substances in the treatment of malaria. Radical cure of an individual infection is not a simple expression of the efficacy of the specific treatment, but is influenced by the immune response of the individual and by inherent characteristics of the causative species or strain of malaria parasite. The mechanism of species and strain differences is in large part explained by the probable existence of an exo-erythrocytic cycle of development of the human parasite. Malaria relapses may be the result of parasitic activity in the exo-erythrocytic cycle, or of renewed activity in the erythrocytic cycle. Chemotherapeutic agents in general use exhibit a highly selective action on erythrocytic forms or on exo-erythrocytic forms of the parasite, but not on both—except perhaps paludrine. New concepts promise to provide a more rational and better understanding of the many difficult problems involved in the treatment of relapsing malaria.

Norman White

PINTO, G. de S. O tratamento da malaria cronica recidivante. [**Treatment of Chronic Relapsing Malaria.**] *Folha Med.* 1947, July 5, 11 pp.

CRAIGE, B., Jr., JONES, R., Jr., WHORTON, C. M., PULLMAN, T. N., ALVING, A. S. & EICHELBERGER, Lillian. **Clinical Standardization of Pamaquin (Plasmochin) in Mosquito-induced *Vivax* Malaria, Chesson Strain. A Preliminary Report.** *Amer. J. Trop. Med.* 1947, May, v. 27, No. 3, 309–15. [11 refs.]

These observations on the value of plasmoquine in the treatment of *P. vivax* malaria have proved useful as a standard for the appraisal of the toxicity of other 8-aminoquinolines. The tests were made on presumably susceptible, white, male volunteers in the Illinois State Penitentiary, a non-endemic locality. Treatment was begun promptly after the onset of the primary attack, or early relapse, of mosquito-induced *P. vivax* malaria, Chesson strain. In one series of observations quinine dihydrochloride, or sulphate, was given concurrently with plasmoquine; in another, an eight-day course of quinine sulphate followed the completion of the plasmoquine course. In all cases, the dose of the quinine salt was 2·0 gm. daily (divided into doses at intervals of 4 hours). Plasmoquine naphthoate was used: the dosage is expressed in terms of plasmoquine base, which is 45 per cent. of the weight of the naphthoate salt. The daily doses of plasmoquine base administered varied from 15 to 63 mgm. The duration of the plasmoquine course was generally 14 days: ten patients were treated for 28 days with 15 mgm. of plasmoquine base a day.

When plasmoquine was given for 14 days, followed by quinine for eight days, every patient relapsed. When both drugs were given together, several patients failed to relapse but complete protection was not obtained. Three of five patients receiving 15 mgm. plasmoquine base and 2 gm. quinine sulphate a day for 28 days relapsed. The subsequent latent period was longer after the larger doses of plasmoquine.

With 15 mgm. plasmoquine base a day there were practically no toxic symptoms; methaemoglobinaemia was only 3 per cent. of total haemoglobin; with 63 mgm. a day abdominal pain, anorexia, nausea and vomiting were frequently severe, necessitating discontinuance of treatment; methaemoglobinaemia 12 per cent. The average percentage of total haemoglobin converted to methaemoglobin was found to be a useful measure for the comparison of the toxicity of various regimes of plasmoquine administration. *Norman White*

INNES, J. **The Chemotherapy of Benign Tertian Malaria.** *Edinburgh Med. J.* 1947, June, v. 54, No. 6, 284–95.

This is a lecture based on work done in an Army Malaria Research team 1944–46 on cases of benign tertian malaria seen in the Mediterranean area, and on others from the Far East. There were 700 cases, the great majority being caused by benign tertian infections acquired in the Mediterranean area, where the troops were taking suppressive mepacrine. It was decided to concentrate on parasite findings in treated persons as a result of laboratory studies, rather than on the comparison of results obtained with different drugs and treatment régimes. Parasites were counted in proportion to white blood cells, with white cell counts estimated per cmm. at intervals of 24 hours. The stage of development of the parasite was also recorded.

In the majority of cases, most of the parasites were at the same stage of development at one time. In others, the members of two cycles could be easily distinguished. Fewer parasites were seen in fresh B.T. infections than in relapsing ones. The oral administration of quinine (10 grains t.i.d.) or mepacrine (low dosage being 0·2 gm. t.i.d. for 24 hours; then 0·1 gm. t.i.d.; and heavy dosage being 0·2 gm. q.i.d. for 48 hours; then 0·1 gm. t.i.d.) resulted in an average duration of parasitaemia of less than 2·5 days from the beginning of treatment in fresh infections. In relapses treated with quinine plus pamaquin (10 grains plus 0·01 gm. respectively t.i.d.), mepacrine (0·2 gm. t.i.d.) or

paludrine (250 mgm. t.i.d.) there was a clearance of the blood parasites in less than 2 days. Pamaquin given alone (0·01 gm. t.i.d.) was followed by parasitaemia for 3·1 days.

The following changes were observed in the asexual cycle of the parasites with all drugs: (1) slowing down of rate of development of the various stages; (2) tendency of large ring and amoeboid form to "collapse"; (3) bunching together of pigment; and (4) destruction of one or more of the parasite stages in the asexual cycle.

The following changes were attributed to the specific drug taken: *Quinine* had a rapid action. The maximum killing effect seemed to be exerted on merozoites and the youngest trophozoites. *Mepacrine* also had a rapid action. A collapse of amoeboid trophozoites, bunching of pigment and destruction of schizonts occurred. A single dose of 0·2 gm. given by intramuscular injection at the pre-schizont stage usually caused a rapid clearance of parasites and had a lethal effect on the schizonts. *Pamaquin* was a slow-acting drug; it was schizonticidal and active in its effect on merocytes [merocytes are red cells containing merozoites]. Sometimes extrusion of pigment was caused before the parasite matured. The author believes that it is this liberation of pigment which results in the occurrence of a clinical malarial paroxysm. The powerful schizonticidal action of pamaquin is perhaps not widely recognized; and it is noteworthy that the daily dosage of the drug (30 mgm.) is 20 to 30 times smaller than that of mepacrine required to produce an equivalent result. *Paludrine* acted on the early schizonts and interfered with chromatin division. The forms which were produced persisted, and resembled female B.T. gametocytes. Paludrine did not clear the blood of benign tertian gametocytes.

Patients were followed up for a minimum period of six months, many of them for longer. In all, 450 cases were followed up. Of every 10 who had relapse infections and were treated with quinine and pamaquin for 10 days, 8–9 were cured. The relapse rate in patients from the Far East treated with 250 mgm. of paludrine plus pamaquin 0·01 gm. t.i.d. were also low, though these drugs together proved toxic. In more than 200 patients to whom pamaquin was given at some stage of the illness, the relapse rate was significantly lower than in those to whom other drugs, but no pamaquin, were given. A series of 50 patients with multiple B.T. relapses treated with an intermittent dosage of quinine plus pamaquin over a period of 30 days did not relapse in one single instance.

[This paper reviews the experiences of a team working on infections produced by at least two strains or varieties of *P. vivax*. This is a factor which must always be remembered when various régimes of treatment are compared. In the main, the findings are similar to those of previous workers on this subject. Many of the cases were drawn from a population taking suppressive mepacrine, but no indication is given about the regularity of its administration. There is no direct suggestion that the strains in this (Mediterranean) area were resistant to mepacrine. Little support will be found for the assertion that malarial pigment, released at schizogony or as the result of treatment, is responsible for the malarial paroxysm. The results obtained with the group consisting of returned prisoners of war from the Far East should be considered with reserve, as here a considerable degree of immunity must have been present. Some of the statements warrant adequate documentation before comment can be made.]

Robert H. Black

De, M. N. & Dutta, P. N. **A Clinical Study on Paludrine.** *Indian Med. Gaz.* 1947, May, v. 82, No. 5, 257–60.

Fifty-eight patients admitted to Medical College Hospital, Calcutta, with active malaria and parasitaemia were treated with paludrine [presumably

orally]. Twenty of these had M.T. infections and the remainder B.T.; none had recently had any other antimalarial treatment. The blood was examined for parasites every 24 hours. Patients in Group I (4 M.T. and 8 B.T.) were given 1 " tablet " [? 100 mgm.] of paludrine thrice daily for 7 days and then twice daily for another 7 days. " Parasites " [presumably asexual] vanished from the blood within from 48 to 96+ hours and the temperature dropped to normal within from 12 to 80 hours in these cases. Group II patients (6 M.T. and 14 B.T.) were given 1 " tablet " thrice daily for 7 days. In these cases " parasites " vanished from the blood in from 24 to 72+ hours and the temperature subsided within from 12 to 96 hours. Group III patients (1 M.T. and 13 B.T.) received 1 " tablet " twice daily for 7 days. " Parasites " vanished from the blood in from 24 hours to 72+ hours, and the fever subsided within 24 to 72 hours in all but two cases (both B.T.) in which it persisted for 120 hours.

Group IV cases were all severe, with very heavy parasitaemia (4 M.T. and 3 B.T.). These received 2 " tablets " thrice daily for 2 days, and then 1 " tablet " thrice daily for 5 or 6 days. Those patients who were too ill to swallow the tablets were given them, crushed and suspended in fluid, through a nasal tube. In these cases the " parasites " vanished in from 48 to 72+ hours, and the temperature subsided within 24 to 84 hours.

Group V cases, five in number, were not treated personally by the authors, and received 1 " tablet " thrice daily for 3 days. [No data are given relative to these.]

No toxic effects from the treatment were observed in the 58 cases; and no relapses were encountered within an observation period of 2 to 3 weeks. The authors consider that paludrine is an effective drug and that " so far it appears to hold out fair prospects of being effective against relapse ", but [wisely] add that the period of observation is inadequate to justify a final conclusion on this matter. *A. R. D. Adams*

CHAUDHURI, R. N. & RAI CHAUDHURI, M. N. **Clinical Trials of Paludrine.** *Indian Med. Gaz.* 1947, May, v. 82, No. 5, 247–53, 9 figs.

Eighty patients (chiefly Indian) admitted to the Carmichael Hospital, Calcutta, suffering from acute malarial attacks of less than a week's duration, who had " fair " or " large " numbers of parasites in their blood, and who had not received antimalarial treatment prior to admission, were treated with paludrine orally. Forty-seven of these had *Plasmodium falciparum*, 30 *P. vivax*, 2 *P. malariae*, and 1 mixed *P. falciparum* and *P. vivax* infections. The dosages employed were as follows :—

Age in years ...	Above 12	6 to 12	Under 6
Regime A... ...	100 mgm. (1 tablet)	50 mgm. (½ tablet)	50 mgm. (½ tablet)
Regime B... ...	300 mgm. (3 tablets)	150 mgm. (1½ tablets)	100 mgm. (1 tablet)
Regime C... ...	(1 tablet t.d.s. for 4 days)	(½ tablet t.d.s. for 4 days)	(½ tablet b.d. for 4 days)

All became afebrile and free from asexual parasites within, at most, 5 days (full data are given in figures, charts and tables).

The *average* periods within which the temperatures became normal and the asexual parasites disappeared from the peripheral blood after treatment were as follows :—

Regime	Duration of fever	Duration of asexual parasites in blood
A ...	3 days	2·6 days
B ...	2·4 days	2·4 days
C ...	2·5 days	2·3 days

In those treated under régime A (7 M.T. ; 2 B.T. ; 1 Q. ; and 1 mixed M.T. and B.T. infections) asexual parasites had vanished in 82 per cent. and the temperature had fallen in 73 per cent. of the cases within 3 days ; under régime B (26 M.T. ; and 16 B.T.) these results were achieved in 88 per cent. and 88 per cent. ; and under régime C (14 M.T. ; 12 B.T. ; and 1 Q.) in 93 per cent. and 89 per cent. respectively.

There was evidence of more rapid action of the drug in *P. falciparum* infections than in those due to *P. vivax* ; gametocytes of neither species were destroyed by the drug ; but mosquitoes fed on two patients with gametocytes (*P. falciparum*) 4 or 5 days after treatment did not become infected. The relapse rates in 39 patients (24 M.T. ; 12 B.T. ; 2 Q. ; and 1 mixed M.T. and B.T. infections) observed for 2 to 4 weeks after treatment were high, especially among the cases of M.T. malaria treated with régime A or B ; none (6 M.T. ; 2 B.T. ; and 1 mixed M.T. and B.T. infections) of the 39 patients treated with régime C relapsed within these periods of observation.

The authors conclude that paludrine has an action on clinical malaria comparable with that of quinine or of mepacrine. A dosage of 100 mgm. of paludrine thrice daily for 4 days is more effective than either a single dose of 100 mgm. or one of 300 mgm. in arresting an acute attack of malaria. No untoward effect was observed in any patient which could be attributed to the drug. *A. R. D. Adams*

PAREKH, J. G. & BOGHANI, B. P. **Clinical Trial of Paludrine in Malaria.** *Indian Med. Gaz.* 1947, May, v. 82, No. 5, 253–5.

Fifty patients admitted to the Sir J. J. Group of Hospitals, Bombay, suffering from acute malaria infections were treated with paludrine [presumably orally] after at least one rigor had been observed in each case. These were made up of 26 cases of B.T., 20 of M.T., and 3 of Quartan malaria ; there was 1 mixed M.T. and Q. infections.

The dosages of paludrine employed were (1) 100 mgm. (single dose) ; (2) 300 mgm. (single dose) ; (3) 100 mgm. daily for from 2 to 8 days ; (4) 100 mgm. once weekly for from 2 to 24 weeks ; (5) 100 mgm. thrice daily for from 2 to 10 days ; and (6) 200 mgm. thrice daily for from 3 to 5 days. In most of the cases treated, even those with a single dose of 100 mgm. (7 B.T. ; and 3 M.T.), the dosage was effective in arresting the paroxysm usually within 24 hours, but sometimes it took longer (in a case of M.T. getting 100 mgm. weekly asexual parasites persisted for 6 days and the fever for 9 days after the first dose of the drug). Two persons suffering from M.T. malaria died of cerebral complications within 4 hours and 6 hours, respectively, of receiving each a single dose of 300 mgm. of paludrine. In 48 of the 50 persons treated, asexual parasites vanished from the peripheral blood, usually in 1 to 3 days after the start of treatment. Gametocytes of all three species, often in increased numbers, persisted in the blood for from 4 to 20 days (and in a case of B.T. infection for 90 days) after treatment. Among 25 patients followed up for 3 weeks to 9 months (15 B.T. ; 7 M.T. ; 2 Q. ; and 1 mixed M.T. and Q.) after the various treatments there were 7 relapses ; these occurred in 1 of 3 M.T.

cases treated with a single dose of 100 mgm. (these were followed up for at least 4 months); in the only B.T. case treated with 100 mgm. daily for 8 days (followed up for 3½ months); in 4 of 6 B.T. cases treated with 100 mgm. weekly for from 2 to 24 weeks (followed up for from 5 to 9 months); and in 1 of 2 B.T. cases treated with 100 mgm. thrice daily for 3 days (followed up for from 5 to 7 months). Data relative to the dosages, types of infection and subsequent history of the patients are given in a table.

Six patients were considered to have shown toxic manifestations due to the drug, but these were unrelated to the size of the dosage, and were attributed to personal idiosyncrasy to the drug. The manifestations included weakness and drowsiness, diarrhoea and vomiting, pains in the back and urticarial eruptions with desquamation. The authors, on their results, consider paludrine at least equal, if not superior, to other antimalarials in the clinical cure of malaria. *A. R. D. Adams*

i. Bull. U.S. Army Med. Dept. 1947, Oct., v. 7, No. 10, 834–5. **Chloroquine-Diphosphate—a Newly-Standardized Antimalarial Drug.**

ii. ——. pp. 835–7. **Clinical Evaluation of Chloroquine.**

i. Successful results in the United States and elsewhere with the antimalaria drug chloroquine (SN 7618) have already been reported [this *Bulletin*, 1946, v. 43, 708, 1011; 1947, v. 44, 502, 792]. The Medical Department of the U. S. Army has now adopted this product as a standardized "improved malarial therapeutic and suppressive drug." It is dispensed as tablets of 0·5 gm., equivalent to 0·3 gm. of base. The nature and effects of the drug have already been described in the abstracts quoted above. It is noted that the standard dosage adopted for the initial attack or an acute relapse is one 0·5 gm. tablet, followed 4 hours later by a second, this dose of 0·5 gm. being repeated at 9 a.m. next morning and at the same time on two further days. A total dosage is thus given in 4 days of five 0·5 gm. tablets (2·5 gm.) containing 1·5 gm. active base. This dosage should not be exceeded. As a suppressive, a single dose of one 0·5 gm. tablet is given weekly.

With this schedule, the attack is usually controlled promptly and the parasites removed from the blood in less than 24 hours. The interval between relapses is considerably longer than when quinine or mepacrine is used. Signs of toxicity are few, mild and rarely require discontinuance of the drug. The only troublesome manifestation noted with frequency of any significance was pruritus without rash in less than 10 per cent. of patients treated. Anorexia, mild nausea and vertigo occurred but were rare. The announcement adds that the removal of atabrine [mepacrine] from the list of standard items is not contemplated at present.

ii. This report records the results of clinical trials of chloroquine on 1,322 patients in U.S. Army hospitals, under standardized conditions. *P. vivax* was present in 1,277, *P. malariae* in 44, and one patient was treated on clinical findings only. No *P. falciparum* infections are included. Data regarding previous attacks treated with other drugs were available in 896 cases. Of these, 90 per cent. had suffered from one or more relapses. Sixty-five patients had had relapses after previous treatment with chloroquine; 54 of these occurred after a single treatment only. In 1,077 patients of whom the relevant data were available, 5 per cent. were afebrile on admission, 64·6 per cent. became afebrile within 24 hours, 23·7 between 24 and 48 hours and 6·6 per cent. after 48 hours. In 700 patients, it could be recorded that 59·7 per cent. became free of parasites within 24 hours, 29 per cent. between 24 and 48 hours, and 8 per cent. between 48 and 72 hours. The remaining 2·7 per cent. did not become parasite-free until after 72 and under 96 hours. Of all the 1,322 patients,

21·4 per cent. showed one or more reactions attributable to the drug. Pruritus accounted for 124 of these reactions, anorexia for 86, vertigo or tinnitus for 76, diarrhoea for 33, and urticaria and malaise for 4 and 3 respectively. [Even though they were generally mild and rarely required discontinuance of the drug, reactions attributable to the drug to the extent of 21 per cent. do constitute an undesirable feature.] *H. J. O'D. Burke-Gaffney*

KAMAL, A. M. & ABDEL MESSIH, G. **Aralen. A New Antimalarial Compound, SN 7618.** Reprinted from *J. Egyptian Pub. Health. Ass.* 1947, Apr., 31–6.

The authors record a clinical study of Aralen (the Winthrop Products' trade name for chloroquine, SN 7618) on similar lines to that previously reported, also from Egypt, by HALAWANI *et al.* [this *Bulletin*, 1947, v. 44, 792]. The drug was administered to patients in the Damanhur and Tanta Fever Hospitals in two schedules. The study was confined to new attacks, not relapses. Aralen is supplied in 0·25 gm. tablets. Schedule A consisted of an initial dose of 1 gm. (4 tablets) followed by 0·5 gm. six hours later, and again after a further 24 and 48 hours. Thus 2·5 gm. (10 tablets) were given in 3 days.

In Schedule B, 2 gm. (8 tablets) were given in equal doses of 0·5 gm every 4 hours.

Forty-five patients (39 benign and 6 subtertian infections) were treated on Schedule A. In 35 of the benign cases, treatment was given in a morning afebrile period in expectation of an attack. In 22 of them, the attack occurred in the afternoon, but the temperature returned to normal next morning and remained thus until the patients were discharged 12 days later. In 13, the attack was prevented and no subsequent attacks occurred. In the remaining four, treatment was given when the temperature was raised: in all, it dropped to normal in 12–24 hours, but a second attack occurred within a further 24 hours. In 33 per cent. of the cases, therefore, the normal temperature was maintained, and in all the cases, cure of the acute attack occurred within 24–48 hours.

In the 6 subtertian cases, one patient maintained the initial normal temperature, 2 became normal in 24 hours, 2 between 24 and 48 hours and one within 72 hours.

Eight patients with benign tertian malaria were treated on Schedule B. Of these, 4 maintained their initial normal temperatures, 3 became normal in 24 hours and one suffered an attack the next day. Thus, acute clinical attacks were cured within 24 to 48 hours in almost every case whether the drug was given on one or over 3 days. This is considerably shorter than the time required for treatment with quinine or mepacrine.

In a table, the authors compare their results with "American experience" of mepacrine and Aralen, which indicate that their own findings in the case of the latter drug in respect of its effect on temperature correspond fairly closely with the American experience [the "American experience" on which these figures are based is not indicated].

In studying "parasite clearance", the blood of 28 patients under treatment with Aralen was examined twice daily for 12 days. In benign cases on Schedule B, trophozoites and gametes [*sic*—evidently gametocytes] disappeared from the blood of the 8 patients concerned within 48 hours of treatment. In 15 patients on Schedule A, only 5 were negative in 48 hours, 7 became negative in 72 hours and 3 after 96 hours. Thus only 33 per cent. of patients were free of parasites within 48 hours, compared with 98·3 per cent. in "the American experience". It is, however, emphasized that all the 8 patients on Schedule B became parasite-free in 48 hours.

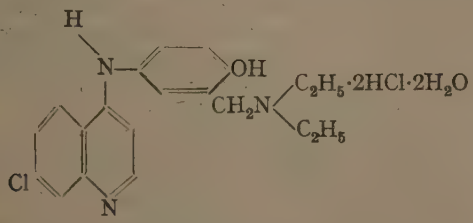
In subtertian infections [numbers not stated, but presumably 5], trophozoites disappeared within 72–96 hours, but "gametes" were not affected.

Only 8 patients in the whole series were followed up : no relapses were noted at the time of writing (20 to 48 days). There was very little toxicity in this series : one patient suffered from headache and one from brief vomiting. [Compare with U.S. Army Medical report above.]

H. J. O'D. Burke-Gaffney

SIMEONS, A. T. W. & CHHATRE, K. D. **Preliminary Report on a New Synthetic Antimalarial.** *Indian Med Gaz.* 1947, May, v. 82, No. 5, 255–7.

" Cam-Aqi ", 4 (3' diethylaminoethyl 4'-hydroxyanilino)-7-chloroquinoline dihydrochloride dihydrate, is a yellow crystalline powder soluble to the extent of 1 gm. in 5 cc. of water at 25°C. Its structural formula is as follows :—



This compound was found by the Parke Davis Research Laboratories to be " several times as effective as quinine and quinacrine " in " avian malaria " ; absorption from the gut was very rapid and high plasma levels were rapidly reached [? in birds]. The acute toxicity in laboratory animals was about that of quinacrine [mepacrine], but the chronic was one-quarter to one-half that of mepacrine. Anorexia, vomiting, spasticity, clonic convulsions and respiratory failure were produced only by prolonged dosage several times greater than in the case of mepacrine. The excretion of the drug from laboratory animals was slow.

In view of these observations, *viz.*, its rapid absorption, rapidly achieved high plasma level, slow excretion, low toxicity and therapeutic efficiency " in laboratory animals ", the drug was considered suitable for trial in single oral dosage in human malaria, 10 mgm./kilo. body weight being the dosages selected.

Fifty men from the Kolhapur State Forces suffering from clinically acute malaria (39 *Plasmodium vivax* and 11 *P. falciparum* infections), most of them with heavy parasitaemia, were hospitalized. Two-hourly temperature records were kept ; for the first 48 hours a tablet of ascorbic acid was given thrice daily as a placebo ; a single dose of " Cam-Aqi " (10 mgm./kilo.) was then given by mouth ; and the blood was thereafter examined at intervals of ½ to 4 hours as long as parasites persisted in it. In the 39 B.T. infections, asexual parasites vanished from the blood in an average of 25 hours (max. 46 hours) and in the 11 M.T. infections, 23 hours (max. 40 hours). The fever in both infections subsided within 48 hours. Circulating crescents were not obviously affected, but there was no evidence of further gametocyte formation ; this is ascribed to the action of the drug on the exoerythrocytic stages of *P. falciparum*. No relapses, clinical or parasitic, were observed among these 50 men over a period of 3 months continuous observation. No toxic effects attributable to the drug were encountered among them, or among a number of non-malarial patients suffering from cirrhosis of the liver, severe anaemia, advanced tuberculosis, nephritis and typhoid, to whom equivalent doses were given.

Sixteen patients (10 *P. vivax* and 6 *P. falciparum* infections) were then treated with 7·5 mgm./kilo., and 18 (8 *P. vivax* and 10 *P. falciparum*) with 5 mgm./kilo. of the drug. The results are summarized in the following table :—

Dose, mgm./kgm.	Number of cases		Relapses observed		Average time required for the clearance of peripheral blood (in hours)		Average time required for the temperature to subside (in hours)	
	B.T.	M.T.	B.T.	M.T.	B.T.	M.T.	B.T.	M.T.
10	39	11	Nil	Nil	25	23	28	27
7·5	10	6	Nil	2	25·5	35	25	35
5	8	10	2	7	32·5	32	35	41

From this it is evident that the rapidity of action diminished with the dosage, and that relapses occurred increasingly with the lowered dosage, particularly in the M.T. infections. The authors conclude that 7·5 mgm./kilo. is an adequate dosage in B.T. infections, but inadequate in M.T.; 5 mgm./kilo., while it arrests the attack, is inadequate to prevent relapse in either infection. A few patients were given 15 mgm./kilo., with enhancement of the rapidity of action in arresting the clinical disease, but this benefit did not appear to offset its increased cost; no evidence of toxicity was noted with the bigger dose.

One hundred and ten children boarding in a Mission School Hostel suffered from much malaria, up to 20 being absent daily with microscopically diagnosed malaria. Every child in the Hostel was given a dose of "Cam-Aqi" (between 5 and 7·5 mgm./kilo.); within 3 days clinical malaria vanished from the Hostel and remained absent for 2 months, when the children went on holiday. On their return, two had overt malaria, probably relapses, and were treated with 10 mgm./kilo.; no further cases occurred over a period of 5 months. Another 116 day boys at the school, with a similarly high malaria incidence, were given 10 mgm./kilo. of the drug; no further cases occurred over 2 months' observation. No toxic effects were seen in any of these children.

For field purposes, where it is impracticable to weigh individuals, the authors suggest the following dosages:—

Infants up to 2 years	½ tablet	0·1 gm.
Children from 2–5 years	1	,, 0·2 gm.
Children from 5–14 years	1½	,, 0·3 gm.
Average South Indian adults ...	2	,, 0·4 gm.
Tall or heavy adults	3–4	,, 0·6–0·8 gm.

The authors consider "Cam-Aqi" a real advance in malaria therapeutics, especially for employment in rural population.

[In the "Survey on antimalarial drugs 1941–1945", edited by WISELOGLE (J. W. Edwards, Ann Arbor, Michigan, 1946, see this *Bulletin*, 1947, v. 44, 1106), Vol. I, p. 398, and Vol. II, Pt. 2, p. 1165, may be found a description of the similar compound, S.N. 10,751, with an account of its chemistry, antimalarial activity in screening tests, mammalian pharmacology, and clinical investigation. For a preliminary report on "Cam-Aqi", see also this *Bulletin*, 1947, v. 44, 698.]

A. R. D. Adams

CHRISTOPHERS, S. R. **Mosquito Repellents. Being a Report of the Work of the Mosquito Repellent Inquiry, Cambridge 1943-5.** *J. Hygiene.* 1947, May, v. 45, No. 2, 176–231, 6 figs. [Numerous refs.]

This is a full and well-documented survey of the whole subject of mosquito repellents, and summarizes all previous work, as well as describing the careful experiments carried out in Cambridge during the war. Previous work had been badly standardized, and, frequently, impure samples of alleged mosquito

repellents had been used in which small quantities of impurities had been responsible for the effects obtained.

The author explains that it is necessary to carry out laboratory tests rather than field tests, to obtain strictly comparable results. He also stresses the importance of having a " standard insect " and gives details of methods of breeding *Aëdes aegypti* for that purpose.

The paper contains detailed accounts of experiments with a very large number of different preparations containing substances alleged to repel mosquitoes, and also with a large number of pure substances. Various methods are given for making the anti-mosquito effect last under tropical conditions and when the skin is rubbed. There is an account of the effectiveness of impregnating fabrics with mosquito repellents, and a discussion of the protection given to the skin by closely woven fabrics.

Those concerned with research into the question of mosquito repellents are referred to the original paper which, although it is over 50 pages long, is still a summary of the work, and further condensation is impossible. The practical applications are as follows. Pure dimethyl phthalate is still probably the best repellent for mosquitoes and midges. It should be applied to all the exposed skin in a thin film. Creams containing dimethyl phthalate, several formulae of which are given, give good results, and a little Java citronella incorporated in the cream may keep the mosquitoes at a distance from the skin so that a complete covering is not so necessary.

Finally, the author stresses the fact that there is still much research to be done before a perfect mosquito repellent is discovered, and it should be remembered that different species of insect may react differently to the same chemical substance, which may give good protection against one mosquito and little or none against another. *Kenneth Mellanby*

NAGENDRA, S. **Futher Observations on Dry Leaf Packing for the Control of Mosquito Breeding.** *Indian J. Malariology.* 1947, Mar., v. 1, No. 1, 67–79.

From the results of regular larval catches the author shows that there is much less mosquito breeding in portions of streams controlled by dry-leaf packing than in the sections where canalization is the sole control measure ; he attributes this to the creation of a mechanical barrier against oviposition by mosquitoes. No observations were made prior to the institution of control measures, and the anopheline larvae subsequently caught were not identified. *R. Ford Tredre*

RAO, V. V. & RAMAKRISHNA, V. **De-Weeding Tanks and Ponds in Antimalaria Operations.** *Indian J. Malariology.* 1947, Mar., v. 1, No. 1, 51–66, 3 figs. on 1 pl. & 3 text figs.

In several areas in India, vector *Anopheles* breed in still water associated with aquatic vegetation ; such waters may be many acres in extent, rendering their control by chemical larvicides too expensive a proposition for the local villages. The obvious method of control is by removal of weeds, but the authors draw attention to the disadvantages of this, of which the principal is the production of turbidity in previously clear water, rendering it apparently unfit even for domestic purposes ; coincident with this is the rapid spread of the algal growth, *Microcystis*. To restore the purity of the water, the authors recommend the planting of the common aquatic herb, *Ottelia alismoides*, which inhibits the spread of *Microcystis* and limits the growth of other major plants.

Manual removal of weeds may be obviated by (*a*) the introduction of silt-laden river water, or (*b*) salinification by saline waters, where these measures are

possible ; freshwater plants are destroyed in each case. Lastly, the authors are enthusiastic about the value of raising vegetable crops on the beds of the tanks when they are dry in the summer months ; the soil appears to be rendered sterile for the rest of the year and little aquatic vegetation appears when the tanks refill in the wet season. *R. Ford Tredre*

BRADLEY, G. H. & FRITZ, R. F. **Entomological Evaluations of Results of Residual DDT Spraying during 1946.** *J. National Malaria Soc.* 1947, June, v. 6, No. 2, 117–21.

In a previous paper [see this *Bulletin*, 1947, v. 44, 180], the authors describe the highly effective results of residual DDT spraying as observed in some 400,000 homes in the Southern U.S.A., where the spray was applied at the rate of 100 mgm. of DDT per square foot, on one or more occasions. At this time, the authors noted that the " effectiveness of DDT deposits, as measured by the percentage of sprayed houses found free of live mosquitoes, gradually decreased during successive months following application. However, after four months, live mosquitoes were found in only about 8 per cent. of treated houses examined." The present paper describes the continuation of this work in which, during the 1946 season, over 750,000 houses were treated ; but on this occasion the DDT was increased to 200 mgm. per square foot in an effort to secure a more lasting residual effect and thereby to decrease the frequency of application. A comparison of the results of the two forms of treatment are shown in the following table.

House Inspections on Residual Spray Program

Total treated houses inspected and per cent. free of *A. quadrimaculatus* in afternoon

Months after spraying	1946			1945*
	Number houses inspected	Houses free of *A. quad.*		Per cent. of houses free of *A. quadrimaculatus* (for comparison)
		Number	Per cent	
–1	6,018	5,969	99·19	98·9
1–2	6,739	6,673	99·02	98·3
2–3	5,321	5,271	99·06	95·7
3–4	2,974	2,935	98·69	94·7
4+	899	883	98·22	94·2
Total	21,951	21,731		
Per cent. ...			99·00	97·2

*BRADLEY, G. H. and Roy F. FRITZ. 1946. Entomological evaluation of DDT residual spraying for malaria control. *Jour. Nat'l. Malaria Soc.* 5 : 141–145.

In a later table, the authors show that a greater proportion of sprayed houses found to be mosquito-positive occurred in areas with a high *Anopheles quadrimaculatus* density. During the 1946 period, precipitin tests carried out in 25,798 specimens of *A. quadrimaculatus* collected on premises where the houses had been treated with DDT, showed that only 40 (0·2 per cent.) gave reactions for human blood, whilst among 6,509 anophelines collected from untreated premises, 74 (1·1 per cent.) gave a similar reaction. Thus, it is indicated that the proportion of the anopheline population that had fed on human beings and survived was 82 per cent. less around sprayed than around unsprayed premises.

[This paper contains a wealth of information packed into a small space, concerning the effectiveness of residual DDT spraying on *Anopheles quadrimaculatus*, and is of particular interest in view of recently published papers by British workers on similar investigations carried out with DDT and directed against *Anopheles gambiae* in West Africa. Muirhead THOMSON (this *Bulletin*, 1947, v. 44, 795) in an important paper has drawn attention to the repellent action exerted by DDT when used as a residual spray against *A. gambiae* ; and has shown that although this species is not deterred from entering treated habitations, nevertheless, having fed on human beings, it leaves the house without having taken up sufficient DDT to cause its death. HOCKING (*ibid.*, 879) concludes that in East Africa " *A. gambiae* and *A. funestus* tend to leave a lightly treated building, but that with an impregnation of about 200 mgm. per square foot, final mosquito mortality approaching 100 per cent. will be achieved, and that on most surfaces the effect will last for at least 4–6 months unless lime is present."

It would appear from these statements, therefore, that in the case of the American vector *A. quadrimaculatus* and of the African vector *A. gambiae*, control by residual DDT spraying will not be fully efficient unless it results in the deposit of not less than 200 mgm. DDT per square foot.]

R. M. Gordon

LINK, V. B. **A Preliminary Report on Malaria Control by DDT Residual Spraying.** *J. National Malaria Soc.* 1947, June, v. 6, No. 2, 124–30, 5 figs.

It is estimated that during the war over half a million U.S. troops contracted malaria. A certain unknown proportion of these men have now returned as carriers, and have thereby increased the malaria risk to the rest of the population. So far, there has been no evidence of any interruption of the downward trend of reported cases of indigenous malaria, but in order to combat the possible transmission of malaria from returning Service men, an energetic programme directed primarily against the adult mosquitoes [see BRADLEY & FRITZ, above] has been initiated by the U.S. Public Health Service and named the " Extended Malaria Control Program " to distinguish it from the " Malaria Control in War Areas Program ". The latter programme, which was carried on during the war, had the opposite object, *i.e.*, to protect troops in the United States from acquiring malaria from the civilian population. The author is careful to point out that the effect of the extended programme in accelerating the downward trend of malaria in the U.S.A. is difficult to measure, since the decrease was observed long before the introduction of DDT. The present paper deals with two surveys, one in South Carolina and the other in Porto Rico, in which the author estimated the residual effect of spraying with DDT on the parasite rates in the human population.

(1) *South Carolina.* An area adjacent to the Santee Cooper Reservoir was selected. This region was chosen because it represented the " only known high endemic malaria area in the United States. Nearly 20 per cent. of the population showed positive blood films in October 1944." A portion of the area adjacent to the reservoir was divided into approximately two equal parts, each having a population of about 1,500 people of whom 90 per cent. were negroes. One of the areas was used as a control and the other sprayed with DDT. Before the spraying, blood surveys were conducted in October 1944, and in April 1945, while the spraying was carried out in the last two weeks of April 1945, and again during the last two weeks of July 1945. Post-spraying surveys were carried out at monthly intervals beginning in June 1945, and are still being continued. The results of these surveys show that the malaria prevalence in

the unsprayed area rose during the transmission season, but remained at a stationary level in the sprayed area. Apparently no examination was made of the insect vector, which in this region is *Anopheles quadrimaculatus*.

(2) *Porto Rico*. Two villages, selected as comparable, were used in this experiment, one village being left untreated, while the other was sprayed in November 1944, July 1945, and again in November 1945. Three blood film surveys were made; the first in the late autumn of 1944, the second in the spring of 1945, and the third in the late autumn of the same year. The results of these surveys are shown in the following table :—

*Per cent. positive blood slides by age groups, Porto Rico, November 1944 to November 1945**

Survey	Humacao Playa (Sprayed)								
	Under 10			Over 10			Total		
	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.
November, 1944	483	28	5·8	977	57	5·8	1,460	85	5·8
March, 1945 ...	440	15	3·4	762	19	2·5	1,202	34	2·8
November, 1945	406	1	0·2	687	9	1·3	1,093	10	0·9

Survey	Loiza Aldea (Unsprayed)								
	Under 10			Over 10			Total		
	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.	Slides	Pos.	Per cent.
November, 1944	380	21	5·5	891	39	4·4	1,271	60	4·7
March, 1945 ...	276	5	1·8	576	8	1·4	852	13	1·5
November, 1945	292	6	2·0	576	27	4·7	868	33	3·8

*Courtesy of Sanitary Engineer (R) Porter Stephens, C.D.C. District Representative, San Juan, Porto Rico.

The vector of malaria in Porto Rico is *Anopheles albimanus*, which seldom remains within houses except for a few hours during the night. Animal bait traps and light traps, which were used for making collections throughout the year, showed that *Anopheles albimanus* was present in sufficient numbers during the study period to transmit malaria, from one to several hundred of these species being collected from all traps during each night. From the results obtained from these two surveys, the author concludes that spraying of homes with DDT decreases the incidence of human malaria.

[In view of the similarly satisfactory results recorded by Bradley and Fritz, also members of the Communicable Disease Center, when using DDT at a concentration of 200 mgm. per square foot, and basing their conclusions on changes observed in the *A. quadrimaculatus* population, it is unfortunate that the author of the present paper has omitted to mention the concentration or method of application of the residual DDT spray responsible for reducing the malaria incidence in the human population. Such information would be particularly interesting in the case of *A. albimanus*, whose short indoor resting period presumably reduces its chances of acquiring a lethal dose of DDT.]

R. M. Gordon

BANG, F. B., HAIRSTON, N. G., MAIER, J. & ROBERTS, F. H. S. **DDT Spraying Inside Houses as a means of Malaria Control in New Guinea.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, July, v. 40, No. 6, 809–22, 2 charts.

This paper describes the reduction in malaria transmission as a result of spraying houses with DDT in a native village, Motu Motu, on the southern coast of Papua, 150 miles west of Port Moresby. A comparable village two miles away was observed as a control. The villages are on swampy land, which is an excellent breeding ground for *A. punctulatus moluccensis* [*A. punctulatus farauti*] and *A. subpictus*. The thatch houses are built on piles 6 to 8 feet above ground. The floors are of rough-hewn planks, laid loosely together ; the walls are of woven palm leaf, thatch, or bamboo strips. Adult anophelines may be taken in numbers underneath the houses throughout the night. Though malaria is hyperendemic, mosquito infection rates were very low ; anopheline prevalence was, however, extremely high.

All the 126 houses in the experimental village were sprayed in two days. Only the interior of houses was treated, walls, partitions, and the adjoining edge of floor and roof. If the walls were very low, part of the roof was also sprayed. A 4 per cent. solution of DDT in kerosene was used at a rate of 100 mgm. of DDT per square foot. Four months later, the number of *A. punctulatus moluccensis* and *A. subpictus* was less than 5 per cent. of that found in neighbouring villages. In the control untreated village, there was an increase in both parasite and spleen indexes. In the treated village, the spleen index remained the same and the parasite index was slightly decreased. There was no change in the amount of *P. falciparum* infection or of the parasite density in positive smears.

A. subpictus was found infected in nature. [It is an important vector in Celebes.] *Norman White*

JOHNSON, H. A. & GOODMAN, W. L. **DDT in Oil as a Mosquito Larvicide.** *Pub. Health Rep.* Wash. 1947, Aug. 15, v. 62, No. 33, 1191–8.

Oiling to destroy mosquito larvae requires the application of 15 to 30 gallons per acre. Incorporation of DDT very substantially reduces the amount to be applied, and the difficulties of labour and transport. Field experiments in Arkansas were conducted in 1944 and 1946 to explore the new method. The DDT solution in kerosene was applied by means of a hand-atomizer by an operator walking at one or two constant speeds to give between 1 and 3 gallons per acre. A proprietary spreading agent was added at the rate of 0·5 per cent. Results were estimated on dipping counts before and twenty-four hours after treatment. It was observed that, with concentrations of DDT between 0·3 and 1·25, satisfactory kills of larvae of *A. quadrimaculatus* were obtained when about 75 gm. of DDT were applied per acre. Partial kills were obtained with 50 gm. per acre and below. *J. R. Busvine*

SAUTET, J., AUDOUIN, A., LEVAVASSEUR, G. & VUILLET, Jeanine, Mlle. Action sur les larves de moustique, d'une suspension pure de D.D.T. obtenue par les ultrasons. [**Action on Mosquito Larvae of Pure Suspensions of DDT obtained by Treatment with Supersonic Waves.**] *C. R. Acad. Sci.* 1947, Jan. 6, v. 224, No. 1, 66–7.

The use of DDT against mosquito larvae has proved valuable, but the solvents or emulsions used in application are commonly harmful to other aquatic life. Fine suspensions are difficult to produce, but the following method is satisfactory. The DDT is dissolved in benzene, and water is added to it. Then the mixture is treated with supersonic waves (by an apparatus described

in *C. R. Soc. Biol.*, 1946, v. 140, 641), which treatment drives off the benzene and leaves DDT in a very fine suspension. This suspension was lethal to *Culex pyrenaicus* down to one part in ten million within twenty-four hours and nearly as effective towards *Theobaldia longeareolata*. Such suspensions in practice would be unaffected by wind or rain. *J. R. Busvine*

TARZWELL, C. M.; ERICKSON, A. G.; BISHOP, E. L. **Effects of DDT Mosquito Larviciding on Wildlife. Part I. The Effects on Surface Organisms of the Routine Hand Application of DDT Larvicides for Mosquito Control** [TARZWELL]. *Pub. Health Rep.* Wash. 1947, Apr. 11, v. 62, No. 15, 525–54, 9 figs. (3 on 2 pls.). **Part II. Effects of Routine Airplane Larviciding on Bird and Mammal Populations** [ERICKSON]. *Ibid.*, Aug. 29, No. 35, 1254–62, 4 figs. **Part III. The Effects on the Plankton Population of Routine Larviciding with DDT** [BISHOP]. *Ibid.*, 1263–8, 7 figs. (3 on 1 pl.)

These papers are the interim reports of a study undertaken by the U. S. Public Health Service in 1944. Section I represents the first year's work, and Sections II and III that of the second year. There will be a later year's study, mainly on the effects on fish.

I. Quantitative sampling of the surface forms, and counts of the surface forms and of dead organisms on the water surface twenty-four hours after treatment, were the methods used for determining the effects of routine treatment with DDT larvicides.

In general, insects were by far the most sensitive organisms. Applications of 0·1 lb. per acre had a fairly substantial effect if repeated as a routine, especially on such large insects as Dytiscidae, Gyrinidae, Hydrophilidae and Corixidae. Even applications of 0·05 and 0·025 lb. per acre had some noticeable effect if they were repeated regularly, though none of these rates had any pronounced detrimental action in a single application. DDT dust treatments were less severe than DDT-fuel-oil solutions.

The seasonal effects of routine DDT treatments, as indicated by a comparison of the populations of surface organisms in treated and untreated ponds, were marked. There was an increase in numbers of Oligochaeta, Nematoda and Copepoda and a decrease in insects, especially Chironomidae. Although the forms which increased were very numerous it is unlikely that they compensated in bulk or suitability as fish foods for the decrease in insects.

The direct effect on fishes was early observed to be detrimental at rates of 0·4 lb. per acre or more. Routine treatments at 0·1 lb. per acre caused some fish mortality after 3 to 10 treatments. It would appear to be unsafe to use routine treatments of DDT above 0·05 lb. per acre. This rate is safe except for shallow waters treated, all over, repeatedly.

II. The effects of routine (weekly) applications of DDT sprayings by aeroplane were observed in 1945 and 1946 at Savannah River Refuge, South Carolina. The DDT larvicide was applied as a thermal aerosol over two large ponds, and as a spray over two more. Observations on ten islands and six dykes were made on the numbers of birds and mammals found active throughout the season.

The results indicated no significant effects in the numbers of birds, cotton rats, house mice, rabbits or racoons.

III. A special plankton trap and a plankton pump were used to determine the effects of hand applications of DDT larvicide to floating organisms in ponds. The DDT was applied at rates between 0·2 and 0·05 lb. per acre.

The results showed that the effects of DDT were relatively small compared with the variations due to climatic and other ecological factors, and not likely to be important. *J. R. Busvine*

KIKUTH, W. & MUDROW, Lilly. Frühstadien der Vogelmalariaparasiten nach Sporozoiteninfektion. [**Early Stages of Bird Malaria Parasites after Sporozoite Infection.**] *Klin. Woch.* 1939, Nov. 11, v. 18, No. 45, 1443–4, 2 figs.

In this note, the authors discuss the origin of exoerythrocytic schizonts in bird malaria and point out that up to the time of writing the paper under review there has always existed the possibility that they may have originated from erythrocytic pigmented forms. They now note that in experiments with *P. cathemerium* the injection of sporozoites into the pectoral muscle was followed by the appearance of a number of uninuclear exoerythrocytic forms 16 hours after the inoculation. These had blue-staining cytoplasmic bodies and a red nucleus. In addition to these uninuclear forms, two more advanced stages with 2 and 3 nuclei were found. Examination of a bird killed 24 hours after inoculation was negative, but a single uninucleated parasite was found in one killed 40 hours after inoculation. The authors consider that these observations prove that the sporozoite actually develops into non-pigmented exoerythrocytic forms. [This paper, published in 1939, has only recently been received.]

C. M. Wenyon

PARAENSE, W. L. Ação patogênica das formas exoeritrocitárias do *Plasmodium gallinaceum*. 1. Investigações preliminares. 2. Prova terapêutica da ação patogênica. [**Pathogenic Action of Exoerythrocytic Forms of *Plasmodium gallinaceum*. 1. Preliminary Investigations. 2. Therapeutic Test of Pathogenic Action.**] *Mem. Inst. Oswaldo Cruz.* 1946, v. 44, No. 1, 147–92, 7 figs., 6 graphs & 4 pls. (3 coloured). [21 refs.] English summary.

When young chicks were inoculated with sporozoites of *Plasmodium gallinaceum* exo-schizonts appeared before erythrocytic forms, since the former are products of sporozoite division. When parasitized blood was inoculated, the first forms to appear were erythrocytic forms. If quinine treatment was given to the chicks following blood inoculation, the chicks died between the 14th and 17th days when it was found that the brain was teeming with exo-schizonts. On the other hand, the blood infection could not be suppressed, as young trophozoites were always present. The control chicks untreated by quinine all died before the 8th day. In another experiment, 80 5-day-old chicks were each inoculated intravenously with 65,000,000 parasites. Death occurred in the untreated controls in 4 to 6 days, while in the treated group death occurred in 10–15 days. Exo-forms were present in the brain of the treated group but not in the controls, which showed a massive blood infection. Trophozoites were present in the blood of the treated chicks and these increased in number from the 7th day till the time of death, when there were present about 20 per 100 erythrocytes. When the dose of parasites injected was less than 2,800 per bird, all but two of the treated birds died between the 18th and 21st days. Of untreated birds, two died at the peak of the blood infection and neither showed any exo-infection in the brain. The remaining untreated birds survived this period and died between 21st and 24th days with heavy exo-infection of the brain. It seems evident that the resistance to acute infection in untreated birds was equivalent to the action of quinine in treated birds.

In a batch of quinine-treated chicks, examination of the blood and of brain tissue obtained by biopsy was carried out with the object of determining any relationship which might exist between the blood parasites and exo-forms in the brain. The two curves showed a striking parallelism, so that it appears that the increasing trophozoites in the blood of quinine-treated chicks is a d rect result of the exo-forms in the brain. In two chicks, recrudescence of parasites occurred 20 days after the beginning of latency. In these chicks there was the

same parallelism between the number of blood trophozoites and exo-forms in the brain. The lack of schizogonic development of the blood trophozoites, beyond suggesting parasiticidal antibodies, appears to indicate that malarial immunity is stimulated by erythrocytic parasites alone, as the exo-forms were completing their normal development. In all these experiments, it was not possible to eliminate the blood infection and it remains to be proved whether death is due to the blood form or to the exo-stages in the brain.

An attempt was made to eliminate the blood infection by use of sulphadiazine. Ten 5-day-old chicks were inoculated intravenously and given quinine from the 3rd day. On the 8th day, sulphadiazine (1·0 mgm. per kilo of body weight) was given twice daily to 4 of the birds in addition to the quinine. All the quinine-treated birds died between the 14th and 17th days and showed the usual increase of blood trophozoites. The 4 chicks treated with sulphadiazine were examined by brain biopsy on the 4th, 7th, 7th and 8th days of treatment. In the brain of all were found damaged exo-forms, while blood smears were negative, though the presence of a subpatent infection was demonstrated by blood inoculation to healthy chicks. When treatment was suspended, the blood forms increased and all the birds died with heavy exo-infections. In another experiment, the sulphadiazine was given on two or three occasions with the result that there was a greater survival of the birds treated with sulphadiazine and quinine. The finding of altered exo-forms in the surviving birds is an indication of the rôle the exo-forms play in the death mechanism.

C. M. Wenyon

WILLIAMSON, J. & LOURIE, E. M. **Acquired Paludrine-Resistance in *Plasmodium gallinaceum*. I. Development of Resistance to Paludrine and Failure to develop Resistance to certain other Antimalarials.** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 278–91. [30 refs.]

It was recently shown by BISHOP & BIRKETT and by the present authors [this *Bulletin*, 1947, v. 44, 969, 970] that resistance to paludrine, which persisted after passage in *Aëdes* mosquitoes, could be produced in *P. gallinaceum*. The same strain could not be made resistant to mepacrine, quinine, M 3349 or sulphadiazine. The present paper gives further details of these experiments. With the four last-named drugs, chickens 6- to 9-weeks old were used as hosts and serial inoculation was carried out from one treated bird to another. If the birds survived the course, six daily drug treatments per week were given for two weeks after parasites had been detected in the blood. The survivors, except in the case of those which received sulphadiazine, were generally heavily infected with exoerythrocytic forms. After 2½ years of treatment, drug-resistance was not detected.

Six-days-old chicks were used as hosts in the production of a paludrine-resistant strain. One series of birds was treated with the minimum effective dose of drug for the normal strain and a second series with the maximum dose tolerated by the host. Treatment was started on the day of intravenous inoculation with parasitized red cells and was then continued twice daily for 3 days. In the first series, resistance was established after about 3 months and quite suddenly ; in the second series it appeared at approximately the same time as a result, it is believed, of mutation. About 20–40 times as much drug was tolerated by the resistant strains of parasites as by the normal without apparent change in morphology. The resistance to paludrine did not extend to other drugs, except the N_5-methyl derivative. The possible mechanism of production of drug resistance and its significance in the treatment of human malaria with this drug are discussed.

J. D. Fulton

MARSHALL, P. B. **Mode of Action of "Paludrine".** [Correspondence.] *Nature.* 1947, Oct. 4, 463.

HAWKING [this *Bulletin*, 1947, v. 44, 648] has given evidence that paludrine is inactive against malarial parasites *in vitro*, but becomes active after it has undergone some metabolic change in the body. In contrast, Marshall finds that paludrine 1/60,000 produces a greater inhibition of oxygen consumption of *P. gallinaceum* in the presence of glucose or lactate than does quinine 1/6,000. Inhibition of oxygen consumption by paludrine is essentially different from that by iodo-acetic acid. The author suggests that paludrine exerts its anti-malarial action, at least partially, by inhibiting the oxidation processes of the malaria parasite, but not the anaerobic breakdown of glucose to lactic acid. However, the concentrations required to produce these effects are higher than those occurring in therapy or those used by Hawking, so their significance is not yet certain. *F. Hawking*

RIGDON, R. H. **An in Vitro Study of the Mechanism producing Rapid Diminution in the Parasitemia in Ducks infected with** *Plasmodium lophurae.* *Amer. J. Hyg.* 1947, Sept., v. 46, No. 2, 254–9, 3 figs.

Oxygen, nitrogen, and carbon dioxide are bubbled for two hours through citrated blood obtained from ducks infected with *P. lophurae.* The blood is then inoculated into clean ducklings and the degree of parasitaemia is measured in the ensuing infections, the results being compared with an injection of untreated blood as a control. Treatment with carbon dioxide resulted in a lesser degree of parasitaemia than did that with nitrogen or oxygen. The author suggests that the accumulation of CO_2 in the body at the peak of the infection may be the cause of the sudden drop in numbers of parasites following the crisis.

[So many different factors are involved that it is difficult to conclude much from these experiments. The author states in the discussion that one should be careful in assuming that CO_2 is lethal for the plasmodia, and yet in the summary says that "apparently the plasmodia are killed by the CO_2.] *P. C. C. Garnham*

THOMSON, K. J., FREUND, J., SOMMER, Harriet E. & WALTER, Annabel W. **Immunization of Ducks against Malaria by means of Killed Parasites with or without Adjuvants.** *Amer. J. Trop. Med.* 1947, Mar., v. 27, No. 2, 79–105, 15 figs. & 1 pl.

In a previous paper, the authors have referred to experiments showing that it is possible to immunize ducks against *Plasmodium lophurae* with a vaccine consisting of formalin-killed parasites combined with paraffin oil containing killed tubercle bacilli and an emulsifying agent [this *Bulletin*, 1946, v. 43, 311]. In the present paper further details are given. It is possible to immunize adult ducks against infection with *P. lophurae* and *P. cathemerium* by injection of the vaccine. With *P. lophurae* immunity is revealed by prevention of death or by lowering the degree or shortening the duration of parasitaemia and with *P. cathemerium* by modifying the course of parasitaemia. Repeated intramuscular injections protect adult ducks for six months, but single injections with multiple sites protect to a less extent. If the injections are given into the subcutaneous fat and not into the muscle no protection results. In ducks, the inclusion of killed tubercle bacilli in the vaccine gave rise to amyloidosis of the liver and spleen, but this did not influence the immunity in any way. In monkeys immunized against *P. knowlesi* by vaccine containing killed tubercle bacilli amyloidosis did not occur. *C. M. Wenyon*

RIVERO, M. D. La infección experimental por el *Haemoproteus columbae* Celli y Sanfelice. [**Experimental Infection with** *H. colombae.*] *Medicina.* Mexico. 1947, May 10, v. 27, No. 531, 197–204, 9 figs.

Two views exist as to the method of transmission of *Haemoproteus columbae* from pigeon to pigeon. According to ARAGÃO, species of *Lynchia* infect themselves by taking up blood from an infected bird. In the intestine, flagellation of the male gametocyte occurs and the fertilized female becomes an oökinete. This discards its pigment and as such is inoculated to the pigeon. According to ADIE, the oökinete in the intestine of the *Lynchia* penetrates the wall of the stomach and develops into an oöcyst, giving rise to sporozoites which invade the salivary glands.

In order to test these views, the author has followed the development of the parasite in larvae of *Triatoma.* This proceeds as far as the formation of oökinetes but no further. With the contents of the stomach of triatomas 24, 48 and 72 hours after feeding on an infected pigeon, uninfected pigeons were inoculated intravenously. From the 12th to the 20th days after the inoculation, the blood showed invasion by young gametocytes which during the following two months developed into mature forms. It is evident that the oökinetes are able to start an infection as ARAGÃO had maintained. [See also this *Bulletin*, 1941, v. 38, 568.] *C. M. Wenyon*

TRYPANOSOMIASIS

FAIRBAIRN, H. **The Infection of Rats by Trypanosomes** (*T. rhodesiense*) **taken from Man early in the Disease.** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 218–25, 1 fig.

In this work the author has continued to study the relation between the electric charge carried by trypanosomes and the results obtained in experimental trypanosomiasis [see this *Bulletin*, 1947, v. 44, 649]. A single strain of *Trypanosoma rhodesiense* (isolated in 1934 from a human case) was used, but "lines" of the strain had been maintained in sheep, Thomson's gazelle, and monkey, by cyclical transmission through *Glossina morsitans.*

Tsetse flies infected with one or other of these "lines" were allowed to bite human volunteers. Fluid from the site of the bite was examined daily and, when trypanosomes first appeared, blood from that site was used to inoculate rats and to prepare films for studying the morphology of the trypanosomes. In the same way, when trypanosomes showed in ordinary blood films, venous blood was taken for blood films and for rat inoculations.

Four types of results were obtained in the rat experiments. In Group I, all rats became infected after the usual incubation period of 4–8 days; in Group II, all rats became infected after an increased period of incubation (9–18 days); in Group III, some rats were infected after incubation periods varying from 8–50 days and others remained uninfected; in Group IV, all rats remained healthy.

The length distributions of the 6 types of trypanosome recognized by the author (long, intermediate, short, each either positively or negatively charged) were determined from the blood films. All types were present in each group, though in different proportions, but only the long type need be considered. By the author's hypothesis the other types cannot initiate infection, for which both the positively and negatively charged forms of the long type are required. From previous observations, the normal mean length for the positive form of *T. rhodesiense* is 29μ and for the negative form 28μ. In Group I, a considerable

proportion of individuals had lengths greater than the general mean: in Groups II, III and IV the proportion was progressively less. Relating this finding to the result of the rat experiments, the author suggests that trypanosomes whose length is above the mean are "mature." They alone can enter into syngamy and produce infection. [The author and his co-worker CULWICK are putting forward new concepts on trypanosomiasis, so it is their duty to plan their experiments in such a manner that the results provide unequivocal evidence for or against their hypothesis. The experiments detailed in this communication fail, in the reviewer's opinion, to achieve this end. Why is it important to test the virulence to rats of the trypanosomes on their first appearance in the blood? No reason is advanced. No consideration is given in the author's discussion of his results to an apparent relation between the "line" of the trypanosome and its virulence to rats. For instance, Table I shows that of 144 sheep-line-man-rat tests only 51 (35 per cent.) were positive, whereas of 69 monkey-line-man-rat tests 65 (95 per cent.) were positive. The fact is noted that no comment is made. Then when dealing with syngamy of the long forms, the statement is made that the argument does not apply to syringe-passage strains which consist only of long forms, although their mean length is reduced. Inoculation of a single trypanosome of these strains will produce infection, and this is taken to mean that genetic segregation has taken place, since conjugation to produce short and intermediate forms cannot occur. Surely this is assuming the correctness of the hypothesis which the experiments are supposed to be testing.] *J. C. Broom*

VANDERPLANK, F. L. **Experiments in the Hybridisation of Tsetse-Flies** (*Glossina, Diptera*) **and the possibility of a New Method of Control.** With Appendix I by W. H. POTTS. *Trans. Roy. Entom. Soc. London.* 1947, June 30, v. 98, Pt. 1, 1–18, 8 figs. on 2 pls. [12 refs.]

The author writes about what would perhaps be better described as "cross-pairing" rather than "hybridisation" between two closely related species of tsetse *G. morsitans* and *swynnertoni*.

The virgin female tsetse is attractive to the male very early in life and pairing takes place either before or very soon after the first meal: after pairing the female ceases to be attractive to the male for the rest of her life. The author finds that if both sexes of these two species are kept together in a cage, mating is random: that is to say, the number of matings with an individual of the same and of the other species is determined by abundance, and there is no "preference" for a partner of the same species.

When pairing takes place, either with a male of the same or of the opposite species, the female is generally, though not always, inseminated. If the pairing has been with a male of the other species, she is in effect sterilized, for she ovulates in a normal way but the eggs fail to hatch: as a somewhat rare event the egg will hatch and eventually give rise to a normal pupa. The hybrid that emerges from such a pupa resembles *G. swynnertoni* in its external characters, whichever species may have supplied the mother. In the case of a male hybrid, it is found that the genitalia exhibit intermediate characters: no similar differences can be shown in females, which are in any event indistinguishable in these closely related species. The hybrids are themselves sterile.

The author shows that in nature the two species overlap in certain areas, in which a few males with intermediate genitalia occur. As such individuals are never found except where the two species are present, one is justified in regarding them as hybrids. He also shows that if large numbers of *morsitans* are introduced into an area inhabited solely by *swynnertoni* cross-pairing

occurs and occasional hybrids are produced. It is likely, therefore, on the basis of the laboratory work, that many other females have been inseminated by the male of the introduced species and are thereby sterilized (though this is not actually demonstrated). The method might perhaps be used to attack a species in nature, especially if the numbers have been brought to a very low level by some other method. The method could only be employed where the introduced species would be able to live in the environment in which it is liberated but could probably not occupy it permanently. *P. A. Buxton*

NATURE. 1947, Oct. 11, 485–6. **D.D.T. and the Aeroplane in the Control of the Tsetse Fly and Trypanosomiasis in South Africa.**

The note describes a meeting in London in September 1947, at which Dr. P. J. DU TOIT discussed recent South African work against tsetse and showed a film.

The particular problem was the control of *Glossina pallidipes* in a small game reserve in Zululand. In the most recent work, an attempt is made to control this insect by DDT smoke, obtained by discharging a concentrated solution into the hot exhausts of aircraft, and sublimating the insecticide, which then falls and is found to penetrate dense bush. The smoke was put down by Anson aircraft, flying cross wind at 120 m.p.h.: the effective swathe was 70 yards at wind speeds of about 6–10 m.p.h. At any one moment a large proportion of the tsetse population is in the pupal stage in the soil: the smoke was therefore put down on six occasions over a period of weeks. The cost of insecticide for six occasions is given as 12s. per acre, and the cost of aircraft services as 6s. [which is surely a token figure].

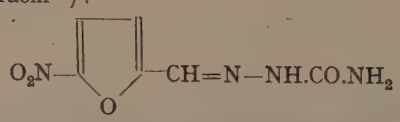
In broken ground, with ravines, where low flying would be exceptionally difficult, DDT smoke may be produced by small generators placed by a ground party.

The catches after spraying were "exceedingly low," but no figure is given. Harris traps have in years past also made an enormous reduction in the same insect in the same area, but never exterminated it. [The speaker was, it seems, rather optimistic: he hoped that, a very great mortality having been produced, nature would step in and do the rest.] *P. A. Buxton*

i. DODD, M. C. **The Chemotherapeutic Properties of 5-Nitro-2-Furaldehyde Semicarbazone (Furacin).** Reprinted from *J. Pharm. & Exper. Therap.* 1946, Apr., v. 86, No. 4, 311–23. [10 refs.]

ii. KRANTZ, J. C., Jr. & EVANS, W. E., Jr. **A Contribution to the Pharmacology of 5-Nitro-2-Furaldehyde Semicarbazone.** *Ibid.* 1945, Dec., v. 85, No. 4, 324–31, 1 chart.

i. It has been found that a nitro group in the 5-position confers definite antibacterial properties on a variety of 2-substituted derivatives of furane. The most promising of an extensive series examined was 5-nitro-2-furaldehyde semicarbazone ("Furacin"):—



"Furacin" is active not only against a wide range of bacteria *in vitro* and *in vivo*, but also against *Trypanosoma equiperdum* infections. Its activity against bacteria embraces both Gram-positive and Gram-negative organisms,

as well as *Myco. tuberculosis*, but it is conspicuously without effect against *Ps. pyocyanea*, and is only very slightly active against *Str. viridans* and *Str. pneumoniae*.

The compound is only slightly soluble in water (1/4,200), and for therapeutic tests, carried out in mice and rats, it was administered as a suspension in 10 per cent. gum acacia, by stomach tube, or in 10–20 per cent. gum acacia subcutaneously or intravenously. Details are given of successful results in infections with two Gram-positive bacterial species (*Staph. aureus* and *Str. haemolyticus*) and two Gram-negative species (*Salm. paratyphi B* and *Salm. typhi-murium*).

There was a fairly high degree of activity against *T. equiperdum* infections, the following therapeutic indices being given, where treatment was by stomach tube :—For mice : LD50/CD50, 9. For rats, LD100/CD100, 8.

Histological examination of organs from animals sacrificed after oral treatment with maximal dosages failed to reveal the pathological basis for the drug's toxic action at high dosage-levels. However, maximal subcutaneous doses gave rise to severe hepatitis and extensive degeneration of the tubular epithelium of the kidney.

[There is an important gap in the data on this compound's performance against *T. equiperdum* infections. The tests against bacterial infections generally showed the curious feature that a dose of about 150 mgm. per kgm. orally produced the maximal therapeutic effect, whilst larger doses—though still well below the lethal range—gave significantly poorer results. For example, in *Staph. aureus* infections in mice, survival-rates after dosages of 150, 200 and 250 mgm./kgm. were 63·3, 36·7, and 40·0 per cent. respectively ; again, in *Salm. paratyphi B* infections the rates were 58·3, 61·7 and 33·3 per cent. respectively. Deaths after treatment by the highest dose were the result of infection and not of toxic action of the drug. In the protocols given for tests against *T. equiperdum* infections, however, no results are recorded for doses higher than 150 mgm./kgm. for mice and 100 mgm./kgm. for rats.]

ii. Standard pharmacological and biochemical techniques were employed in order to determine the toxic potentialities of " Furacin." The observations included studies of the effects of the compound on blood pressure, respiration, and the heart-beat as shown by electrocardiogram and by direct observation during perfusion or after extirpation. The effects on cytochrome oxidase and tissue dehydrogenase activity were also studied. Acute and chronic toxicity tests in rats, mice and monkeys were supplemented by blood counts and histopathological studies on the organs of animals which had received the highest dosages.

These tests revealed a very low degree of toxicity. Several persons were given 100 mgm. orally three times a day, without symptoms being produced. The dose was increased to 2–4 gm. daily, which resulted in nausea in 20 per cent. of cases. There were no changes in the blood or urine of these persons. [The numbers treated are not stated.] [See also *Bulletin of Hygiene*, 1946, v. 21, 614.] *E. M. Lourie*

PINTO, C. Epidemiologia da doença de Carlos Chagas no Estado do Rio Grande do Sul—Brasil. [**Epidemiology of Chagas's Disease in the State of Rio Grande do Sul, Brazil.**] *Mem. Inst. Oswaldo Cruz.* 1946, June, v. 44, No. 2, 363–400, 26 figs. (3 maps).

After briefly describing the physiographical features of the State, the author relates that Sanitation Posts have been established in 78 of the 92 municipal districts and that during the 8 years, 1939–46, 73 cases of Chagas's disease have been observed ; the largest number in any single year was 27 in 1942. *Triatoma infestans* is the vector. *Eutriatoma rubrovaria* is found in the burrows of the

armadillo, *Dasypus hybridus*, in the open fields during the winter in temperatures about zero Centigrade. Of the total cases 48 were in children, 22 in adults; in 3 the age was not known. Forty-seven were acute, of whom 38 were children, 7 adults, 2 not known, and of 25 chronic cases [this makes a total of 72 only] 11 were children and 14 adults. As regards nationality, 38 were whites, 4 negroes, 3 mulattos, but as many as 28 were not known. In all the acute cases, Romaña's sign was present and in 13 there was some cardiac disturbance—tachycardia, arrhythmia, extra-systoles or signs of myocarditis. Diagnosis was made either by direct blood examination or by xenodiagnostic methods. Details as to nationality, age, sex, clinical characters, etc., are given for each patient, in a table. The houses were infested with *Triatomidae* and these were often found collected under the mattresses in the cold weather.

The article contains several maps of the district, photographs of the country, and meteorological and epidemiological details in graphs.

H. Harold Scott

MAYER, M., PIFANO C., F. & MEDINA, R. Aspectos epidemiológicos de la enfermedad de Chagas en Venezuela. Bases para una campaña de saneamiento aplicable a zonas endémicas del medio rural Venezolano. [**Epidemiological Aspects of Chagas' Disease in Venezuela.**] *XII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora. No. 30.* Caracas. 1946, 56 pp., 1 map.

MUNIZ, J. Do valôr da reação de precipitina no diagnóstico das formas agudas e sub-agudas da "Doenca de Chagas" ("Trypanosomiasis Americana"). [**A Precipitin Reaction in Diagnosis of Acute and Subacute Forms of Chagas's Disease.**] *Brasil-Medico.* 1947, July 19 & 26, v. 61, Nos. 29/30, 261–7, 1 graph & 1 fig. English summary.

The author, with his colleague DE FREITAS, has previously published articles dealing with immunity reactions in Chagas's disease [see this *Bulletin*, 1945, v. 42, 975; 1947, v. 44, 571], complement fixation and agglutination. In the present paper he describes a precipitin reaction. The method of obtaining the extract is very detailed and those interested must consult the original; suffice it here to say that, by employing Fuller's method, he obtained from cultures of *T. cruzi* a stable, water-soluble fraction. A very small quantity of serum is needed and the results seem, in the author's hands at least, to be very satisfactory. 0·1 cc. of serum (which must be quite clear and free from blood) of the suspected patient is placed in a small tube of 3 mm. diameter; an equal quantity of precipitinogen is added down the wall of the tube to form a layer over the serum. A control with physiological saline is put up at the same time. The tubes are left at room temperature. In strongly positive cases, a disk appears at the surface of contact in 1–2 minutes (4 plus); less acute cases give the reaction in 10–20 minutes (3 plus), or even longer, after half an hour (2 plus). In a table are given details of 21 cases, stating the length of interval since infection occurred, the results of the precipitin test and the agglutinating titre of the serum. The ages of the patients ranged between 7 months and 14 years. In most, the tests were made more than once at intervals up to 176 days after the date of infection. Adding these cases of acute disease to 12 previously noted, the author states that in every one of the 33 the reaction was positive in the early weeks of infection and remained so for periods up to 4 months. The test is, therefore, of special value in the early stage before definite symptoms appear and takes less time than a search for trypanosomes in the blood, and a positive result is not given by leishmaniasis patients (though immune sera prepared against leishmanial diseases do react). The reaction is of some quantitative value, because it occurs, as a rule, when the agglutination

titre is 1 : 500 or over. It has little value in chronic cases ; only 18 per cent of more than 200 such patients gave a positive. For these chronic cases, other methods, such as complement fixation or xenodiagnosis, are better.

H. Harold Scott

MUNIZ, J., NOBREGA, G. & DA CUNHA, M. Ensaios de vacinação preventiva e curativa nas infecções pelo *Schizotrypanum cruzi*. [**Attempts to vaccinate against *T. cruzi* Infections.**] *Mem. Inst. Oswaldo Cruz.* 1946, Sept., v. 44, No. 3, 529–41. English summary.

Though the results were on the whole negative, this investigation was one of interest. It is known that inoculation of cultures of *T. cruzi* into rabbits results in the formation of specific antibodies, their serum agglutinating in titres up to 1 : 50,000. The authors have utilized Rhesus monkeys, *Macaca mulatta*, because infection of *T. cruzi* in them evolves very like that in man. They tested the value of the vaccine (killed by merthiolate 1 : 10,000) prophylactically and curatively after infection ; inoculation was made intradermally, subcutaneously, intramuscularly and intravenously. The details are given minutely in a series of protocols and described in the text. Those interested should study the original ; suffice it here to repeat what has been said above that the vaccine proved neither protective nor curative in doses of 24–28 mgm.

H. Harold Scott

LEISHMANIASIS

ROMAN, E. Phlébotomes tunisiens de Tebourba et d'Ain-Draham. [*Phlebotomus* **from Tebourba and Aïn-Draham, Tunisia.**] *Ann. Parasit. Humaine et Comparée.* 1947, v. 22, Nos. 1/2, 68–74, 3 figs. [13 refs.]

A study of 543 *Phlebotomus* specimens in north Tunisia revealed the presence in Tebourba of *Phlebotomus minutus parroti*, *P. perniciosus*, *P. longicuspis*, *P. perfiliewi* and *P. papatasi* : the first three species also occur at Aïn-Draham. Aberrant forms are described. The possible local rôle of these species as vectors of leishmaniasis is discussed. *H. J. O'D. Burke-Gaffney*

MACIEL, P. & ROSENFELD, G. Leishmaniose visceral Americana—Um caso de um novo fóco. [**A Case from a New Focus of American Visceral Leishmaniasis.**] Reprinted from *Rev. Clin. São Paulo.* 1947, May–June, v. 21, Nos. 5/6, 51–61, 4 charts, 1 fig. & 1 map. [36 refs.]

DE BARROS, O. M. & ROSENFELD, G. Leishmaniose visceral Americana. Novo caso. [**A New Case of American Visceral Leishmaniasis.**] Reprinted from *Rev. Clin. São Paulo.* 1944, v. 15, No. 4, 97–102, 5 figs. (3 on 1 pl.)

KATZENELLENBOGEN, I. **Cutaneous Leishmaniasis in Palestine with a Report of a New Endemic Focus in the Negev.** *Harefuah*, Jerusalem. 1947, Sept. 14, v. 33, No. 6. [In Hebrew 98–100. (17 refs.) English summary 100.]

Revivim-Asluj, in the Negev, is a new Jewish settlement in Palestine with "sand-desert" conditions. There are some 30 settlers there, and between September 1946 and January 1947, 25 of them developed oriental sores of a "dry" type after a residence of 1 to 2 years. The sores also occur in nomad Bedouin in the neighbourhood of Revivim, but are absent in the case of settlers and nomad Arabs in other parts of the Negev.

The salinity of the soil is high (0·25 to 1·0 per cent.), huge open reservoirs for rain water were built recently and there is a large cave in the settlement, which has been used as a "rest house" by nomads for centuries. Thus, conditions in Revivim favour the breeding of sandflies.

It is not considered that the spread of oriental sore in Palestine can be attributed to carriers from the Dead Sea area or from neighbouring countries, but it is presumed that latent foci of leptomonas-infected sandflies exist and that Revivim is one. Outbreaks of cutaneous leishmaniasis occur in Arabs and Jews alike when non-immune persons enter the area, as has already occurred in the Dead Sea. *H. J. O'D. Burke-Gaffney*

PAVLOV, P. Recherches sur la leishmaniose du chien. Deuxième publication. [**Studies in Canine Leishmaniasis. Second Report.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 7/8, 258–63.

HAMPTON, J. W. F. **The Excretion of Stilbamidine and some related Compounds in Experimental Animals.** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 226–33. [16 refs.]

Studies on the excretion of stilbamidine by human subjects have previously been reported in this *Bulletin* [1943, v. 40, 122; 1945, v. 42, 18] as well as similar investigations on laboratory animals [*ibid.* 1946, v. 43, 723]. In the present paper, the excretion of this substance and of a hydroxy-, amino- and iodo-derivative in the urine of rats and rabbits, has been investigated after single or repeated doses. Stilbamidine itself was estimated by a modification of the fluorescent method of HENRY & GRINDLEY [this *Bulletin*, 1943, v. 40, 122] and also by the glyoxal method of FULLER [this *Bulletin*, 1945, v. 42, 264], after extraction of the bases from urine in butyl alcohol. Amino-stilbamidine was estimated by fluorimetric and diazotization procedures, iodostilbamidine colorimetrically and the hydroxy-derivative by the yellow colour of the base after its extraction by butyl alcohol, other methods having proved unsuitable.

After a single intravenous injection of stilbamidine, only about 1 per cent. of the administered dose was recovered in fluorescent form; about twice this amount was recovered after repeated dosage. When the dose injected was small, excretion could not be detected till 5 doses had been given; after 10 doses there was a sudden rise in the amount present in urine, suggesting that storage had been taking place in the body. The curious observation was made that "proportionately very much less of the compound was excreted by the animals receiving large doses than by those receiving small doses, when the reverse was expected".

The results of colorimetric estimation of stilbamidine indicated an excretion 20 times greater than that found by the fluorimetric method. In the case of aminostilbamidine, higher results for excretion were obtained by the diazotization than by the fluorimetric method. Stilbamidine thus appears to be excreted largely in the form of a non-fluorescent (compound), the identity of which was not established. [When discussing the reason for the low excretion values found for stilbamidine by the fluorimetric method of estimation, the author incorrectly attributes to the reviewer the view that the addition of water occurs at the ethylenic linkage in stilbamidine when its solutions are exposed to light. Recently FULTON & DUNITZ [this *Bulletin*, 1947, v. 44, 988] have shown by X-ray crystallographic methods that dimerization occurs with the formation of a cyclobutane derivative.] *J. D. Fulton*

THOMPSON, R. H. S. & WHITTAKER, V. P. **Antidotal Activity of British Anti-Lewisite against Compounds of Antimony, Gold and Mercury.** *Biochem. J.* 1947, v. 41, No. 3, 342–6, 1 fig. [20 refs.] [Summary appears also in *Bulletin of Hygiene.*]

BAL protects the isolated pyruvate oxidase system of pigeon brain from poisoning by compounds of antimony, gold and mercury. Its antidotal potentialities *in vivo* may therefore be inferred. The compounds examined were :— Antimony : Tartar emetic, " Stibophen ", and " Stibacetin ". Gold : Gold chloride, " Myocrisin ", and 1,aurothioglucose. Mercury : Mercuric chloride. [For other references to BAL in arsenical intoxication see *Bulletin of Hygiene*, 1946, v. 21, 658, 737, 864 ; 1947, v. 22, 189, 511.] *E. M. Lourie*

FEVERS OF THE TYPHUS GROUP

MACKENZIE, M. **Typhus Fever in England.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Oct.–Nov.–Dec., v. 38, Nos. 10–11–12, 873–4. [French version 871–2.]

Typhus fever is now rare in England and Wales, but during the war years special precautions against its importation became necessary. These included the provision of a panel of expert consultants ; the selection of isolation hospitals as special centres ; arrangements for disinfestation of homes and contacts ; the formation of special sanitary teams ; provision of facilities for immunization of exposed medical and sanitary workers ; the supplying of DDT and sprays to Local Authorities and the issue of a memorandum on louse-borne typhus fever.

Two types of yolk-sac vaccine were provided, one (Cox type) prepared by the U.S. Public Health Service and the other by the Connaught Laboratories, Toronto. Facilities were provided for the inoculation of authorized travellers abroad.

During the war, until 1944, only two suspected cases of typhus were reported in England and Wales. One was probably of the tick-borne type and therefore of no local epidemiological importance. The other was in a soldier who became ill a few days after an anti-typhus inoculation : in this case, the diagnosis was not confirmed as a result of serological tests.

The danger increased after the invasion of Germany and VE day, especially as regards the risk of infection being carried by returning prisoners of war. In fact, 21 such cases were imported, 14 in ex-prisoners of war and 7 in medical students returning from voluntary duty in Belsen. Measures taken to prevent secondary cases were successful and none occurred thereafter.

H. J. O'D. Burke-Gaffney

BOYER, J. **Epidemiological Study of Cases of Typhus Fever found in the Paris Area on the Return of Prisoners and Deportees.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Oct.–Nov.–Dec., v. 38, Nos. 10–11–12, 865–70. [French version 855–64, 5 graphs.]

Among prisoners and deportees who returned to France in 1945, there were 167 cases of typhus fever in Paris, which was the main centre for dealing with repatriated persons. There were only 15 secondary cases among persons who came in contact with the patients after their return to Paris. In four of the

secondary cases, the only contact had been with repatriated persons who had never suffered from fever, and who, therefore, were assumed to have suffered from "inapparent" attacks of the disease.

Plans had already been made for prompt diagnosis of cases and for the disinfestation and disinfection of all contacts, who were kept under close observation for 25 days instead of the 12-day period prescribed by international regulations. Contacts were not vaccinated because they ceased to incur risk of infection after detection, but nurses, doctors, and officials of the Repatriation Service were vaccinated with the Durand and Giroud vaccine. Only one vaccinated person was attacked, and she made a good recovery.

John W. D. Megaw

DIAS, A. de C. **Typhus Fever in Portugal during the War Years.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Oct.–Nov.–Dec., v. 38, Nos. 10–11–12, 878–80. [French version 875–7.]

The influx of war refugees and the partial mobilization of Portuguese troops throughout the Portuguese empire exposed Portugal to a number of infectious diseases: of these, typhus in particular was a serious risk, because of the great epidemic in Spain in 1941–42, which demanded stringent precautions along a wide stretch of the frontier. Indeed, of 50 cases which did occur in Portugal in 1941, more than half were traceable to the Spanish epidemic. It was proved that the disease was imported by gypsies, even in the city of Lisbon where typhus has always been rare.

Figures are given of incidence and deaths by ages, in Lisbon and the provinces, between which the cases and deaths were exactly evenly divided (25 and 3 in each respectively). It is noted that in Lisbon, none of the 3 deaths occurred in people over 50, when the severity is greater: in the provinces, 1 death occurred in a person over 50, and 2 in persons of unknown ages.

Cases also occurred in Portugal in 1943 and 1944, in two districts, one coastal and one inland, which were formerly the seats of epidemics. Two small epidemic centres appeared in the northern areas in 1943, and in 1944, epidemics occurred in two other northern and one south coastal area. The last comprised 19 cases only, and it would have been the most serious but for prompt measures taken, since the commune concerned (Othaô) is a populous fishing and fish-canning centre.

The incidence and mortality of typhus in Portugal during the war years is shown in the following table:—

Year	Cases	Deaths
1939	33	10
1940	6	6
1941	50	8
1942	18	14
1943	57	5
1944	124	21
Yearly averages 1929–1938	48·1	12·6

It is noted that unusually high death rates are recorded in 1940 and 1942, but the author attributes the low case incidence to non-notification and considers that the figures are more accurate for years when typhus occurred in epidemic form.

The yearly average for 1929–1938 was slightly exceeded in 1941 and 1943 and more than doubled in 1944. War restrictions, especially the lack of soap, are held to explain the manifestations of typhus in exposed areas.

The intensity of infection was variable. In Othaô in 1944, two deaths occurred in 19 cases. Clinically, among the various degrees of intensity, it is stated that the most frequent form was " typhus *levissimus*".

The orthodox measures were taken and included isolation, delousing, organization of centres, use of 10 per cent. DDT, inspection of incoming travellers and (from 1941) vaccination of sanitary staff with Cox-type vaccine imported from the United States. *H. J. O'D. Burke-Gaffney*

RAYNAL, M. J. H. Les rats et les puces du rat dans leurs rapports avec la pathologie humaine à Chang-Hai. [**Rats, Fleas and Human Pathology in Shanghai.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 5/6, 212–38. [39 refs.]

A title such as " Rats, Fleas and Human Pathology " conjures up immediately the subjects of plague and typhus. These are undoubtedly the major concern of a health authority in conducting and continuing large-scale examination or extermination of rats. In addition to these two important infections, an opportunity was afforded of investigating other possibilities of disease transmission from rat to man : Weil's disease, sodoku, salmonelloses, rabies, and melioidosis. Actually the article returns to an old contention of the author [this *Bulletin*, 1938, v. 35, 781 ; 1939, v. 36, 464, 983 and 1940, v. 37, 256, 569], with newer verification, separating both murine epizootic and sporadic endemic typhus due to murine rickettsiae which are flea-borne, from the occasional outbreaks of epidemic typhus, spreading to man from rats, but which is afterwards louse-borne. Plague as a current problem may be dismissed from consideration (though not its potential dangers in times of unusual prevalence of *Xenopsylla cheopis*), because " it seems that its local implantation is not likely to be easy " and because no case of plague has been detected in Shanghai for twenty years.

As is natural, the preliminary study relates to the rats themselves. The brains of the rats were preserved at —15°C. and, if the Weil-Felix serum test in any individual rat had given a high agglutination titre, the brain was triturated and inoculated intraperitoneally in two guineapigs. In some cases the material served as a test for the existence of rabies which, however, was never discovered. Other materials examined were bone marrow, urine and faeces, tested by culture for the frequency of *Proteus* and salmonellas. The rats were almost all (97 per cent.) of the species *Rattus rattus* (*Epimys* : black house rat) and there were almost no brown sewer rats (*R. norvegicus*). One reason for this may have been that the capture of the rats took place in a business or residential, and not in a port, area. Gravid female rats were found in greatest numbers at the end of winter and in spring. This should be the time to intensify a rat campaign. Males captured bear the proportion to females of 65·6 to 34·3. The fleas captured on rats were *Ctenopsyllus segnis*, *Xenopsylla cheopis*, *Ceratophyllus anisus* and *Ctenocephalides felis* in the relative proportions 62·8 : 26·3 : 10·8 : 0·1. Seasonally, *Xenopsylla cheopis* is prevalent in the warm weather of summer and autumn, and *Ceratophyllus anisus* from February to May. The former, admittedly the rat flea of plague, shows very variable prevalence, and abundance only at long intervals.

Typhus, and by this is meant classical exanthematic typhus in man, made its appearance in epidemic form in Shanghai in the years 1938, 1940 and 1942. This is a common experience in all wartime periods, and is due to crowding, misery and starvation ; the disease manifested itself at an elevated endemic level

from 1938 to 1945. A high correlation, positive or negative as the case might be, with fluctuation from epidemic to endemic, was found between infected rats (diagnosed serologically) human cases of typhus and the number of rat carriers of fleas. In discussing the passage of infection from rat to man the author invokes the existence of very enzoo-epizootic murine localities and of soiled (rat-urine or rat-flea faeces) materials or virulent dust as the agents of transmission. The war conditions mentioned, when the vector becomes the louse and transmission is from man to man, suffice to account for the epidemics of typhus experienced in Shanghai. *W. F. Harvey*

GIROUD, P. & JADIN, J. Mise en évidence par absorption des anticorps du pouvoir antigène des tissus typhiques lavés. [**Antigenic Potency of Washed Typhus-Infected Tissues shown by Agglutinin-Absorption.**] *C.R. Soc. Biol.* 1947, June, v. 141, Nos. 11/12, 579–81.

By means of agglutinin-absorption reactions, it was shown that crushed and washed tissues in which rickettsiae were cultivated retained a measurable quantity of antigen capable of fixing agglutinins [see this *Bulletin*, 1945, v. 42, 366]. *H. J. O'D. Burke-Gaffney*

GIROUD, P. & CIACCIO, G. Pouvoir antigène de divers extraits de poumon de lapin infecté des rickettsies. [**The Antigenic Potency of various Extracts of Rabbit Lung infected with Rickettsiae.**] *C.R. Soc. Biol.* 1947, June, v. 141, Nos. 11/12, 585–6.

Potent antigens were easily obtained in solution from the lungs of rabbits infected by typhus rickettsiae. Of the methods tried the most successful were making suspensions of the lungs, in 10–20 per cent. methyl or ethyl alcohol, in 50 per cent. glycerin, or in 8–10 per cent. sodium chloride.

The solutions when injected subcutaneously into rabbits caused a rapid rise in the rickettsia-agglutination titre of the animals' serum. The solutions, except the one made with glycerin, retained their full potency up to 70 days. After desiccation they also remained stable, with or without preliminary precipitation by ammonium sulphate. *John W. D. Megaw*

VAN DER SCHEER, J., BOHNEL, E. & COX, H. R. **Diagnostic Antigens for Epidemic Typhus, Murine Typhus and Rocky Mountain Spotted Fever.** *J. Immunology.* 1947, Aug., v. 56, No. 4, 365–75. [24 refs.]

The authors begin by giving a useful summary of the various methods of preparing antigens for the complement-fixation tests used in the differential diagnosis of epidemic typhus, murine typhus, and Rocky Mountain spotted fever.

It was found that epidemic and murine typhus vaccines prepared from infected yolk sacs by ether extraction and used as antigens gave non-specific reactions with Wassermann-positive syphilitic sera when the complement-fixation tests were carried out by the specially sensitive method of keeping the preparations at ice-box temperature for 18 hours. Little or no fixation occurred when the vaccines were purified by shaking with benzene and then concentrated by precipitation with sodium sulphate. Rocky Mountain spotted fever vaccines were treated in the same way. It then became possible to differentiate the last-named disease from epidemic and murine typhus, but in some cases epidemic-typhus sera reacted nearly as strongly with murine antigen as with epidemic antigen.

In the three murine-typhus sera that were tested, the reaction against murine antigen was at a much higher titre than that against epidemic antigen.

With antigens prepared from purified and washed rickettsial suspensions by the method described by Plotz, strong cross-reactions were also observed with epidemic- and murine-typhus sera, but the titre was always higher with the homologous than with the heterologous rickettsial antigens.

John W. D. Megaw

i. DELBOVE, P. & REYNES, V. Etude du comportement des virus typho-exanthématiques chez les cobayes tuberculeux. [**The Behaviour of Typhus Rickettsiae in Tuberculous Guineapigs.**] *C.R. Soc. Biol.*. 1947, Mar., v. 141, Nos. 5/6, 210–11.

ii. REYNES, V. & DELBOVE, P. Evolution de la tuberculose expérimentale chez les cobayes surinfectés par un virus typho-exanthématique. [**The Evolution of Tuberculosis in Guineapigs subsequently infected with Typhus Rickettsiae.**] *Ibid.* 211–12.

iii. DELBOVE, P. & REYNES, V. Etude des réactions d'immunité chez des cobayes convalescents de maladie typho-exanthématique et surinfectés avec du Bacille de Koch. [**Immunity Reactions in Guineapigs Convalescent from Typhus and subsequently infected with Tubercle Bacilli.**] *Ibid.* 244–5.

v. REYNES, V. & DELBOVE, P. L'allergie tuberculeuse au cours des fièvres typho-exanthématiques chez le cobaye. [**Tuberculous Allergy in the Course of Typhus in Guineapigs.**] *Ibid.* 245–6.

i. The authors show that in guineapigs infected experimentally with human tubercle bacilli, the course of murine or exanthematic typhus, subsequently induced, differs little from the course in non-tuberculous animals; but the murine strain, which previously had failed to produce the Mooser reaction, regained its capacity to do so, as a result of passage through tuberculous animals. A tropical rickettsial strain [presumably of tsutsugamushi disease] was much less virulent to tuberculosis than to normal guineapigs.

ii. In the second paper the authors show that tuberculous guineapigs later infected with the three strains of typhus rickettsiae lived much longer than tuberculous controls.

iii. In the third paper they claim that if animals which have recovered from infection with the three strains of rickettsiae are subsequently infected with tuberculosis, there is no loss of immunity (within 3–5 months of first typhus infection) when epidemic and tropical [? tsutsugamushi] strains are considered, but that there is loss of immunity in the case of a murine strain. In each case, homologous immunity only is referred to. [The numbers of guineapigs in each group (not more than 10) are so small that it is doubtful if the results are significant.]

iv. Tuberculous guineapigs which are infected with one of the three strains of rickettsiae after their tuberculin reactions have become positive, tend to become negative to tuberculin during the febrile period of the typhus infection, or during convalescence, but return to a positive reaction when recovery from typhus has taken place.

Charles Wilcocks

DELBOVE, P. & REYNES, V. Recherches expérimentales sur l'évolution simultanée de l'infection tuberculeuse et des infections typhoexanthématiques chez le cobaye. [**Experiments on the Simultaneous Infection of Guineapigs with Tubercle Bacilli and Typhus Rickettsiae.**] *Ann. Inst. Pasteur.* 1947, May, v. 73, No. 5, 439–50. [12 refs.]

This is a rather fuller account of the work already reported by these authors in the four papers abstracted above. They were stimulated to conduct this study as a result of several clinical observations, but they do not state what these were.

Charles Wilcocks

LEMKE, R. Über Spätschäden nach Fleckfieber. [**After-Effects of Typhus Fever.**] *Med. Klin.* 1944, Aug. 4, v. 40, Nos. 31/32, 469–70.

Among 150 soldiers examined 4 to 12 months after attacks of typhus fever, about two-thirds complained of one or more of the following symptoms :—cardiac (96) ; irritability and restlessness (74) ; forgetfulness and inability to concentrate (64) ; headache (79) ; weakness (64) ; defects of hearing and ringing in the ears (52) ; and numbness of the limbs (82).

Electrocardiographic abnormalities were detected in only 14 cases, and among these there was seldom any evidence of myocardial damage. There were definite signs of damage to the nervous system in 91 cases, including :—exaggerated tendon reflexes (40) ; clonus and other spastic reflexes (34) ; diminished or absent abdominal reflexes (28) ; inequality of the pupils (45) ; loss of the pupil reaction to light (15) ; nystagmus (25) ; ptosis (15) ; facial-nerve lesions (27) ; hypoglossal-nerve lesions (24) ; Rombergism (16) ; diminution or loss of the knee jerk (17) ; tenderness on pressure over the nerves of the legs (21) ; sensory disturbances in the legs (18) ; and sensory disturbances in the arms (11).

In 32 cases, there was evidence of neuritis, mostly referred to the nerves of the legs. In 76 cases, there were indications of slight damage to the central nervous system.

In 78 cases, the cerebrospinal fluid was abnormal ; in 60 of these there was an increase in the albumin and in 48 there was an increase in the cell count.

Presumably the patients had been selected for special investigation at a nerve clinic ; if so, the figures show only the relative frequency of the various signs and symptoms observed. *John W. D. Megaw*

WEI, H. & WEI, W. P. **Experimental Infection of Silkworm Pupa with Typhus Rickettsia. A Preliminary Report.** *Chinese Med. J.* 1947, May–June, v. 65, Nos. 5/6, 171–5, 2 figs. & 1 chart.

Silkworm pupae were inoculated by the intracoelomic route with murine rickettsial suspensions prepared from the lungs of infected mice. After the pupae had been kept at room temperature for six days, numerous rickettsiae were found in smears made from their tissues. Suspensions of the intestinal and ovarian tubules of the pupae were inoculated into guineapigs, which developed febrile reactions similar to those caused by rickettsial inoculations.

Further study of the behaviour of rickettsiae in silkworms was impossible, because of the war situation that arose in 1944 when the experiments were in progress. *John W. D. Megaw*

WAR OFFICE. **Scrub Typhus Investigations in South East Asia. A Report on Investigations by G.H.Q. [India] Field Typhus Research Team, and the Medical Research Council Field Typhus Team, based on the Scrub Typhus Research Laboratory South East Asia Command, Imphal** [AUDY, J. R., *et al.*] **Part I. General Account.** 58 mimeographed pages of text & 11 Index pages (mimeographed), 1 map, 1 chart & 1 fig. **Part II. Illustrations. Part III. Appendices** (22 papers by individual Workers). 1947. March. London : War Office, AMD. 7.

This important Report deals largely, though not entirely, with wartime investigations carried out by a team of workers at the Scrub-Typhus Research Laboratory, Imphal, near the Indo-Burma frontier.

The output of valuable work by the team was surprisingly large considering that the laboratory was fully staffed only from July to December, 1945, though a few of the workers had been employed from April, 1945, and a rapidly dwindling number remained till March 1946.

Lt.-Col. J. R. Audy, R.A.M.C., the officer in charge of the laboratory, has carried out the formidable task of editing and producing the three substantial volumes which make up the report, and readers will be surprised to find that the whole of this work was done between August 1946, and March 1947, especially as the editor himself has contributed more than half of the text and illustrations.

Lt.-Col. Audy craves indulgence for " many defects " in the report, but his readers will agree that these were inevitable in the circumstances and that they are trifling when weighed against the wealth of valuable material that has been made available to students of the fevers of the typhus group. Considered as a set of collected papers, the only drawbacks to the report are the relegation of the illustrations to a separate volume and the long list of corrigenda and addenda. But the report is much more than a collection of articles as will be gathered from the following review of its contents.

Part i : General Report Account

The opening paper, of 19 pages, is on " The Occurrence and Identification of the Typhus Group of Fevers in the South East Asia Command ". The authors are Col. M. H. P. SAYERS, R.A.M.C., Deputy Director of Pathology, S.E.A.C., and Brigadier I. G. W. HILL, R.A.M.C., Consulting Physician, S.E.A.C. The paper, written in 1945, deals chiefly with the incidence, geographical distribution, epidemiological features, and laboratory studies of scrub typhus in the Eastern Theatre during the years 1941–44. An apology is made for the use of the name scrub typhus, whose only justification is its almost universal adoption ; the classical name is tsutsugamushi fever.

The first outbreak recorded during the war was one of 107 cases seen in 1941 by G. SINGH in a rural area of Central Burma [see this *Bulletin*, 1945, v. 42, 883]. This outbreak, though definitely of the " *OXK* type ", was suspected by Singh to be louse-borne, presumably because mite-borne typhus was not expected to occur as an epidemic.

Little is known of the occurrence of the disease in the area during 1942.

Most of the outbreaks referred to by the authors as occurring in 1943 have afterwards been described in papers by their observers ; they include (1) 121 cases in a battalion of a British regiment not far from Imphal, reported by TATTERSALL and PARRY [this *Bulletin*, 1946, v. 43, 430] ; (2) 500 cases on the India-Burma border in 1943 and early 1944 reported by TATTERSALL [*ibid.*, 28]; and (3) 114 cases of typhus fever of which 96 were of the *OXK* type in an Indian Military Hospital in Calcutta, reported by LUSK [*ibid.*, 246].

The only outbreak of a typhus fever other than scrub typhus mentioned by the authors is one that occurred at Ranchi in Bihar, India, early in 1943. In this, 33 persons became infected in waste-land in January 1943 ; nearly all the patients gave a Weil-Felix response of the " indeterminate type ", none gave an *OXK* reaction, and from the bibliography appended to the paper it appears that B. T. BOWES described the outbreak as one of " Tick-Borne Typhus ".

During 1944 about 5,000 cases, with 350 deaths, are said to have occurred in Burma and Eastern India.

(2) In a brief paper of seven pages, entitled " The Medical Research Council Scrub-Typhus Commission ", Dr. R. LEWTHWAITE, Director of the Institute for Medical Research, Kuala Lumpur, describes the origin and work of the Scrub Typhus Commission established by the Medical Research Council in 1944 ; the original members were, himself as Field Director, with Dr. Kenneth MELLANBY and Charles D. RADFORD as Entomologists. Dr. H. C. BROWNING was appointed in 1945 as Experimental Biologist, but his work was interrupted by an attack of malaria followed by one of scrub typhus contracted in a

hyperendemic area in Burma. Mr. H. T. M. GORDON was appointed as associate to Dr. Browning.

(3) Audy in an article of 26 pages contributes "A Review of Investigations on the Epidemiology of Scrub Typhus in South-East Asia", 1945–1946. This paper, which summarizes the work done by members of the staff of the Imphal Laboratory and other workers, will be found very useful by students of the typhus fevers who have not time to read the whole report. A bibliography of recent contributions on the subject of scrub typhus is appended.

(4) Audy in an article of four pages also describes "The Establishment of the Research Laboratory at Imphal (Manipur)".

(5) A Subject Index (11 pages) to the three volumes of the Report completes Part I.

Part ii

This consists of 135 illustrations reproduced on 69 sheets of foolscap-size art paper.

Part iii : Appendices

This consists of 22 papers, of which 20 are by Lt.-Col. Audy and other members of the Imphal research team, and two are by Dr. M. T. PARKER, late Major, R.A.M.C., from the District Laboratory, Calcutta.

Most of the papers deal with Investigations carried out during the short period of existence of the Imphal Laboratory. The papers can be very roughly classified according to the chief subject matter as Epidemiological, Entomological, Bacteriological, and Survey, but most of them deal with more than one aspect of the disease.

The volume contains more than 200 foolscap-sized pages in small (petit roman) type, and much of the subject matter is of a technical nature so that it is obviously impossible to do justice to each paper. Some of the articles, though published with the consent of the authors, have been collated by the editor from reports and have not been revised by the workers concerned. Several of the papers are expected to be published in complete form at a later date.

Papers dealing chiefly with Epidemiology

In Appendix I (14 pages and 7 illustrations) Audy contributes "A Survey of Scrub Typhus in Burma, 1945". He shows that though previous records of the occurrences of the disease in Burma were scanty, infection was found to be widespread throughout the country and to include such unexpected localities as waste land in urban areas like those of Prome and Mandalay.

In the 12th Army, 586 cases occurred between March and December, 1945. The proved vector was *Trombicula deliensis*, and the chief animal reservoirs were *Bandicota bengalensis* and *Rattus rattus*, though tree shrews and squirrels were of local importance.

Strains of *Rickettsia tsutsugamushi* [now more commonly known as *R. orientalis* : see this *Bulletin*, 1943, v. 40, 828] were recovered from one bandicoot and one rat, in addition to the strains isolated by Kalra from various sources, including patients, and a strain earlier recovered from *T. deliensis* larvae on the Indo-Burma border.

Methods of preventing the disease in peace-time are discussed ; thorough ground clearing followed by cultivation of grazing, and rat control, are likely to be effective, but rat control must be carried out a month or two after the onset of the rains ; earlier operations may increase the risk of transmission by mites and later measures will not reduce the second generation of larvae. Personal protection by dimethyl and dibutyl phthalate and by benzyl benzoate is discussed in general terms.

In Appendix 2 (46 pages and 68 illustrations) Audy presents "An Ecological Study of Scrub Typhus". The ecological features of the disease in areas in Assam, Manipur State, Burma, Ceylon, The Maldive Islands, and India, are described in detail. Statistics of the case-incidence and descriptions of the terrain are supplied for each of a large number of infected localities in which surveys were made.

A section of the paper contains a summary of the factors concerned in the distribution of mites in relation to the ecology of the disease, and another deals with the ecology of the disease in relation to the ecology of the mites and mammals concerned in transmission. In the latter section the reader is confronted with a number of technical terms which the author mercifully defines, otherwise the uninitiated would be puzzled by such names as climatic climax, seral community, subclimax, and scrub constellation.

In Appendix 9 (5 pages) M. T. Parker writes on "Scrub Typhus among Troops in the Calcutta Area in 1942 and 1943". In 1943 there were 195 cases of typhus-group fevers classified as follows: scrub typhus, 150; "*X19* typhus", 23; "indeterminate" (*OX2* type), 4; and "clinical typhus", 18. Most of the cases of clinical typhus were believed to be scrub typhus with a negative Weil-Felix response, and most of the "*X 19*" cases were thought to be murine typhus. [Some of the cases of these two types and the four cases of the *OX2* type may have been tick-borne. Lusk has already discussed the features of the 114 cases of typhus seen in the Indian Military Hospital, Calcutta in 1943 (see this *Bulletin*, 1946, v. 43, 426).] No eschar was seen in any of the cases.

In Appendix 13 (5 pages and 1 illustration) Major S. Lal Kalra, I.A.M.C., Bacteriologist of the General Headquarters, India, Research Team, and Squadron Leader C. D. Radford, R.A.F., describe "Scrub Typhus in Ceylon". Little was known of the existence of the disease in Ceylon till the occurrence of a dramatic outbreak in which 756 persons (713 Africans and 43 British) belonging to a body of troops engaged in manoeuvres in scrub land from 11th to 15th December, 1943, were attacked within a period of seven days from the 22nd December onwards. The mortality rate was 1·3 per cent. among the Africans and *nil* among the British. An eschar occurred in 58 per cent. of the cases.

In a short summary of a paper by Radford on "Scrub Typhus Research in Ceylon" there is a statement of the infestation of bandicoots, rats, shrews, etc., by *T. deliensis* and *Ascoschöngastia indica* Hirst, 1915.

In Appendix 14 (6 pages and 3 illustrations) Kalra deals with "Scrub Typhus Investigations on Addu Atoll, Maldive Islands", and refers to the findings of Radford who collaborated with him in the work.

The most interesting feature of the disease in the small island surveyed was that without the use of mite repellents or vaccines complete control of infection was established by clearing, and keeping clear, the island of all low vegetation. After the initiation of this procedure there was at first a rise in the number of cases, but this was followed by a rapid fall from 33·4 per mille in 1942 to 2·4 in 1944. During the time of the survey—November 1944, to February 1945—there were no cases, and, although rats and shrews infested with *T. deliensis* were found, no rickettsiae could be isolated from the tissues of 111 rats and 32 shrews which were examined. The case-fatality rate was 2·4 per cent. in 600 cases that occurred among Indian troops on the Island.

In Appendix 15 (2 pages) Kalra deals with the "Distribution of Typhus Fevers in India". He has already reported his findings [see this *Bulletin*, 1947, v. 44, 575] but he now rightly states that the "*OX19*" cases presumably include "some tick typhus" in addition to murine typhus, but he still bases his classification of the cases into scrub, murine, and tick typhus, on the Weil-Felix response, which admittedly cannot be relied on to differentiate murine

typhus from tick typhus. [Complement-fixation tests will doubtless throw light on the distribution of the typhus fevers in India.]

In Appendix 16 (7 pages and 4 illustrations), Kalra makes a "Preliminary Report of Typhus Investigations in the Kumaon Hills, United Provinces, India" during the months August to October 1946. In the country round the three small lakes of the Bhim-Tal area, 9 strains of rickettsiae were isolated from 15 rats, and 5 strains were recovered from 17 batches of mites, chiefly *T. deliensis*. Many animals, domestic and wild, including rats, were infested with *Rhipicephalus sanguineus*; and four other species of ticks were found.

More than 2,000 ticks were collected in the region by the "flag" method; different batches of these were inoculated into 23 guineapigs, of which 9 reacted, 4 doubtfully and 5 definitely, including 3 in which there were redness and swelling of the scrotum.

Trombiculid mites and various ticks were found on rats in five other localities, including Almora, where an average of 8 ticks was found on all the 6 rats captured, and 2 of the 3 guineapigs inoculated with separate batches of the ticks reacted with fever and scrotal swelling.

Altogether 20 strains of *Rickettsia tsutsugamushi*, 7 tick-strains related to *Dermacentroxenus* [*Rickettsia*] *rickettsi*, and one suspected murine strain, were isolated in the area of the survey.

In a later Appendix (17, dated February 1947) Kalra gives further details of the investigation of ticks in the Kumaon Hills. Among a total of 20 batches of ticks from various localities, 9 from Bhim Tal, consisting of *R. sanguineus* and *Boophilus* sp., and 3 from Almora, consisting of *Ixodes ricinus*, caused fever and scrotal reaction in guineapigs, and rickettsia-like bodies were found in spleen smears. Complement-fixation tests were carried out with Rocky-Mountain-spotted-fever antigen on the sera of 9 of the guineapigs; 2 of these reacted at a titre of 1–10; both were from animals inoculated with *R. sanguineus* from Bhim Tal, the others gave negative reactions.

In this appendix Kalra also reports the isolation of a similar tick strain of rickettsia from a batch of 11 ticks (*Haemaphysalis leachi* var. *indica*) found on a rat in the Imphal area in November 1945; this rat was also infested with *T. deliensis* mites but these were not infected though the host rat was found infected with *R. tsutsugamushi*.

[These remarkable findings will doubtless stimulate renewed interest in tick typhus in India. The strains of rickettsiae isolated in the neighbourhood of Bhim Tal and Almora will probably be closely studied.]

In Appendix 23 (13 pages and 6 illustrations) H. C. Browning and Kalra present a "Report on a Scrub Typhus Outbreak in the Mandalay Area, May to July 1945."

The number of cases in this outbreak was 103; among 54 cases tested the agglutination responses were aberrant in 6; of these, 3 were of the *OX19* type, 2 were *OX19* combined with *OXK*, and 1 was *OX19* with *OX2*.

A detailed survey was made of the epidemiological conditions. Laboratory mice in cages were exposed in areas in which infection had occurred; among 50 mice 3 became infected with scrub typhus.

An investigation of the fauna of the soil of several localities was carried out by methods described in the paper; Trombiculids were, surprisingly, absent even from the soil of places where experimental mice had become infested or infected, so that the habitat of the nymph and adult forms of the mites remained a mystery.

Papers dealing with Entomology

In Appendix 3 (18 pages and 12 illustrations) Audy discusses "The Biology of Trombiculid Mites in Relation to Transmission of Disease."

The most important observation recorded in this paper is that *T. deliensis* remains attached to its hosts for two to four days, as is the case also with *T. akamushi* of which it may be a variant. This feeding time is shorter than that of species of *Ascoschöngastia* which remain attached for about a week, and much shorter than that of *Walchia* and *Schöngastiella* which have a feeding time of about four weeks. Taking into account the infestation rates of rats in the Imphal area, it is estimated that 3,000–4,000 larvae of *T. deliensis* feed on each rat in a year, so that this mite has a great advantage over other potential vectors which have annual " turnovers " ranging from 800 to only 50 mites.

A summary of this highly instructive paper will be found in the author's Review in Part I.

In Appendix 5 (8 pages and 2 illustrations) Audy and Major H. M. THOMAS, R.A.M.C., Experimental Biologist, contribute a useful " Note on Techniques and Field Collections."

Appendix 7 (6 pages) is by Sergeant T. J. LAWRENCE, R.A.M.C., Entomologist, who writes on " Species of Trombiculid Mites in Manipur and Burma." Many new species described by the author and Radford are included, and opinions on several of these are added by Dr. Henry S. FULLER, formerly attached to the U.S.A. Typhus Commission at Myitkyina.

In Appendix 10 (3 pages) and Appendix 11 (6 pages and 6 illustrations) THOMAS deals with " Observations on the Behaviour of *T. deliensis* in Soil ", and " Observations on the Development of the Nymphophane [pupa] of *T. deliensis*."

These papers will be of special interest to professional entomologists.

In Appendix 19 (5 pages and 7 illustrations) Kalra contributes " Reports on Histological Investigations " in which he describes histological techniques suitable for the investigation of mites in a field laboratory, by making serial sections. The paper includes observations on the internal structure of *T. deliensis*, on the histopathology of the eschar, and on the lesions produced in the skin of the rat by infesting mites.

Appendix 21 is by K. COCKINGS, Entomologist, who, in a short paper of 4 pages with 2 illustrations, deals with " Breeding and Trapping of Trombiculid Mites," and gives details of the technical methods employed.

Papers on Bacteriology and Serology

Appendix 8 (2 pages) is by M. T. PARKER who describes his work on " The Transmission of the infective Agent to Experimental Animals."

In December 1943, the author, working at Calcutta, isolated *R. tsutsugamushi* by inoculating the blood of a patient into the anterior chamber of a rabbit's eye. By the same method, he isolated the organism from the peritoneal exudate of three guineapigs which had been inoculated at Imphal (by Lt. Col. Sayers, R.A.M.C.) with pooled blood clot from several patients. Two other strains were isolated later, one from near Imphal, the other from North Burma, both from guineapigs inoculated intraperitoneally with blood from patients.

Guineapigs inoculated in this way were found very suitable for the transport of strains to distant laboratories.

In Appendix 12 (13 pages and 13 illustrations) Kalra, assisted by Sergeant J. D. BOWER, R.A.M.C., presents a " Report on Field Investigation on Scrub Typhus in Maniput, Assam."

The recovery of 19 strains of *R. tsutsugamushi* from the following sources is described :—(*a*) From patients, 5 strains were isolated by inoculation of blood or blood clot into guineapigs or white mice. The patients were infected in the Imphal or N.W. Burma areas. One of the strains was recovered from the blood of Dr. H. C. Browning on the 4th day of his illness, and a sample of his blood

taken on the 18th day was examined in the U.S.A. by "Dr. Sheppard" [presumably C. C. Shepard], who reported a positive reaction with the complement-fixation test, at a titre of 1–32 against "Gilliam" (Assam) antigen and at a titre of 1–512 against "Karp" (New Guinea) antigen. [Striking variations in the responses of the same sera to different antigens have been reported by BENGTSON (see this *Bulletin*, 1947, v. 44, 61.)]

(*b*) From rats (six strains), from a field-mouse and a tree-shrew (one strain each).

(*c*) From larval mites, six strains were isolated; all the batches of mites employed were collected from rats in the area south of Imphal; two of the strains were from batches of mites consisting solely of *T. deliensis*, the other positive batches were of mixed species, but all contained a certain number of *T. deliensis*.

Strains were also isolated from five of the laboratory white mice that had been exposed to mite attack by being placed in cages on the ground at Mandalay Fort.

Details are given of the extensive work done on the strains; nine of them were maintained for 8 to 20 passages through white mice, in which their virulence usually rose during the earlier passages. Transfers of 14 strains were made from mice to guineapigs, in which various reactions occurred, but only one strain, originating from a tree-shrew, caused peritoneal exudate containing abundant rickettsiae.

A description is given of the varied responses to inoculation of strains into seven rhesus monkeys, obtained from Calcutta and regarded as free from previous infection. Some of the monkeys showed cross-immunity when challenged by a second inoculation with a different strain, but others showed no immunity or only partial immunity.

One monkey, inoculated with a mite strain, developed *OXK* agglutinins up to a titre of 1–320 (on the 34th day); this monkey was again inoculated on the 38th day with the tree-shrew strain already mentioned; the response was a rise in the *OX2* agglutinins, whose titre became 1–1,280 on the 60th day after reinoculation, and a disappearance of the *OXK* agglutinins. This tree-shrew strain did not protect any of four mice from death when they were challenged later by a mite strain. [No mention is made of the possibility that the tree-shrew strain might have been of the tick-borne type; the author states elsewhere that it resembled *R. tsutsugamushi* in its morphology and behaviour in animals.]

Local rats, though regarded as free from the risk of previous infection, were not satisfactory as test animals.

The isolation of a strain from ticks in the area has already been mentioned.

Appendix 17 (8 pages) by Kalra contains "Miscellaneous Supplementary Notes, dated January–February, 1947," in which the isolation of tick strains already mentioned is described. Among other recent studies are the following:—

(1) Three rats were inoculated with strains of *R. tsutsugamushi*, two from Imphal and one from North Burma; six months later the rats were found free from infection and were inoculated with Bhim-Tal strains of the same organism; all three became infected but further experiments are contemplated to find whether infection confers lasting immunity against homologous strains.

(2) Cross-immunity tests were carried out in which rabbits were inoculated intraocularly with strains of *R. tsutsugamushi*, three of which were from the Kumaon Hills, two from Ceylon, and one each from Burma and Imphal. After recovery, the inoculation was repeated with strains from Kumaon; five of the rabbits were found immune, but one of the Ceylon strains and the Imphal strain had conferred no immunity. Immunological differences among various strains are, therefore, suggested.

(3) A list of ticks collected in Imphal and the Kumaon Hills is given; these were identified by Dr. M. SHARIF of the Haffkine Institute, Bombay.

In Imphal the commonest species was *Haemaphysalis leachi indica*, found on rats and tree shrews; the only other tick found on rats was *R. sanguineus*. In the Kumaon hills *R. sanguineus* was the most abundant; it was found on rats, dogs, sheep, cows, and horses; the only other tick found on rats was *Ixodes ricinus*, in Almora.

(4) A note by Audy is included in this Appendix; it is on "An outbreak in Central India, Apparently of Tick Typhus with Eschar". Six persons were attacked in February 1945, in Bhopal State, Central India. Five of the patients had obviously been infected on the same day in a "pin-point area", and all of them had an attack which clinically and serologically conformed to the picture of tick-borne typhus with eschar. The sixth patient was infected a short distance away; he had a similar attack, but without eschar. Audy suggests that the cases with eschar may have been of the boutonneuse-fever type; he states that so far as he knows cases of tick typhus with eschar have not been reported from India. [The reviewer, about 15 years ago, saw a typical case of tick typhus in which there was a pronounced eschar at the site from which the patient had removed a tick just before the onset of the fever; this case was not recorded; the patient was seen in a hospital at New Delhi, by the courtesy of Lt. Col. Aspinall, I.M.S. The presence or absence of an eschar in tick-borne typhus may be fortuitous, just as it is in scrub typhus.]

In Appendix 18 (4 pages) Kalra discusses "The Value of Proteus Agglutinins as an Endemic Index of Scrub Typhus, and in Differentiating Sub-Groups of Tropical Typhus". Sera of many animals captured at Imphal and Addu Attol were tested for the presence of *OXK* agglutinins; a considerable number reacted at titres of 1–20 to 1–80; one flying fox and two lizards reacted at 1–160. Among 30 rats examined, 4 reacted at 1–80, but 4 reacted with *OX19* and 2 with *OX2* at the same titre. No rise in the *OXK* titre occurred among rats inoculated with scrub typhus at Imphal. In a small proportion of scrub-typhus patients at Imphal, Mandalay, etc., atypical reactions occurred and were verified by repeated tests; in most of these the reaction was of the *OX19* type, in a few it was of the combined *OX2* and *OX19* type. The author states that "the clinical disease in all these cases was identical." From these and other findings recorded in the paper, and from a study of the literature, the author concludes that though the Weil-Felix test is a useful aid to diagnosis it "cannot always be relied on to differentiate sub-groups of the disease." [Complement-fixation tests might throw light on the significance of these anomalous reactions.]

Papers on Survey Methods

Appendix 4 (6 pages) is a preliminary report by Audy on "Applications of Air Photography to Research and Survey".

The author claims that air photography is a very useful preliminary to a survey the object of which is to avoid endemic foci of scrub typhus, and that it is also of value in the collection of information for ecological and other investigations. The numerous photographs illustrating Appendix 2 show clearly the kind of information that can rapidly be obtained by air photography.

Appendix 6 (7 pages), also by Audy, deals with "Field Surveys and Methods of Control". Concise instructions are given with regard to the methods and equipment employed in surveying known or suspected scrub-typhus areas. There is also a useful summary of the methods of controlling the disease.

In Appendix 22 (4 pages) BROWNING and GORDON describe "Methods of Field Anaesthesia in Laboratory Mice and Wild Rats". Details are given of the duration of anaesthesia resulting from the administration of several drugs in various doses. Bromethol given intraperitoneally in doses of 0·012 cc.

to rats caused anaesthesia lasting about one hour ; half this dose rendered mice unconscious for about three hours. The drug had the special advantage of quick action, so that when given to animals lightly anaesthetized by chloroform or ether, consciousness was not regained during the brief period needed for the production of its effect. There was also a good margin of safety.

Acknowledgments

Among other acknowledgments, Lt.-Col. Audy and Dr. Lewthwaite express their gratitude for helpful and friendly co-operation by Col. T. T. MACKIE and the other 13 members of the U.S.A. Typhus Commission in North Burma, whose studies of the disease from December 1944, to November 1945, have already been the subject of a preliminary report [see this *Bulletin*, 1946, v. 43, 917 and 1132].

Dr. Lewthwaite also refers to the important work of the Australian entomologists, MCCULLOCH and WOMERSLEY [*ibid.*, 1945, v. 42, 28, 324, and 369]. Valuable contact was made with these workers and also with members of the U.S.A. Typhus-Commission team in New Guinea [*ibid.*, 991 and 993].

John W. D. Megaw

KALRA, S. L. **Inclusion Bodies in** *Rickettsia orientalis* **Infection.** *Indian Med. Gaz.* 1947, June, v. 82, No. 6, 326–7.

In the course of his isolation of 25 strains of *Rickettsia orientalis* from various sources in 1945, the author observed homogeneous intracellular inclusion bodies similar to those described by GIROUD and PANTHIER [this *Bulletin*, 1942, v. 39, 753] as being associated with classical rickettsiae during their adaptation to growth in the lungs of rabbits. The author detected the bodies in epithelial cells in Giemsa-stained smears of peritoneal exudate of mice inoculated by the intraperitoneal route. The bodies were seen in only a few of the strains investigated.

John W. D. Megaw

DAVIS, G. E., AUSTRIAN, R. C. & BELL, E. J. **Observations on Tsutsugamushi Disease (Scrub Typhus) in Assam and Burma. The Recovery of Strains of** *Rickettsia orientalis*. *Amer. J. Hyg.* 1947, Sept., v. 46, No. 2, 268–86.

The recovery of 85 strains of *Rickettsia orientalis* in Assam and Burma has already been described in a preliminary report by MACKIE and other members of the China-Burma-India section of the U.S.A. Typhus Commission [see this *Bulletin*, 1946, v. 43, 917 and 1132].

The authors now give fuller details of their special investigations, including a description of the technical methods employed.

They state that Japanese workers had previously produced evidence of the occurrence of transovarial transmission of *R. orientalis*, but that their own experiments were the first to demonstrate the actual presence of rickettsiae in the tissues of a host (white rat) experimentally infested with laboratory-reared offspring of infected mites (*Trombicula deliensis*). They also claim to have been the first to recover *R. orientalis* from larval trombiculid mites collected from the Yunnan buff-breasted rat (*Rattus flavipectus yunnanensis*) ; from the large shrew (*Suncus murinus fulvo-cinerea*) ; from the Assam tree shrew (*Tupaia belangeri versurae*) ; and from the tissues of the above-named rat and tree-shrew.

The gerbilles—*Gerbillus gerbillus* and *G. pyramidum*—were found superior to white mice for the microscopic demonstration of rickettsiae, especially in primary isolations of the organisms.

John W. D. Megaw

REDDY, D. J. **Scrub Typhus in North Burma.** *Indian Med. Gaz.* 1947, June, v. 82, No. 6, 330–33.

The author has made an analysis of the chief features observed in 68 patients who formed part of "nearly 100 cases" of scrub typhus treated in an Indian General Hospital at Meiktila from May to November 1946.

The nationalities of the patients were: Indian 38, Burmese 19, Japanese 6, and British 5. The fatality rate was 4·5 per cent.; an eschar was seen in 37 per cent., adenopathy in 80 per cent., and a rash in less than 6 per cent.

Apparently the diagnosis was made only in cases in which the *Proteus OXK* titre rose to 1–320 or over at some stage; in 69 per cent. of the cases this titre was reached by the end of the second week. One of the patients had been inoculated against the disease; his attack was mild and his *OXK* titre never rose above 1–320.

An unstated number of inoculated persons were tested weekly after inoculation; their *OXK* titres were found to have "a maximum of 1–40".

During the first week, the majority of the patients showed Widal titres of 1–160 to 1–320, but during the second and third weeks these titres declined.

John W. D. Megaw

GREENBERG, M. & PELLITTERI, O. **Rickettsialpox.** *Bull. New York Acad. Med.* 1947, June, v. 23, No. 6, 338–51, 5 figs. & 2 charts.

This is a clear and succinct description of rickettsialpox, the interesting rickettsial disease whose very existence was not known until the middle of 1946 [see this *Bulletin*, 1947, v. 44, 411; 897].

The authors give an account of the thorough manner in which the disease was investigated within a period of a few months by a team of experts, of which they were members.

The only important feature of the disease that remains unknown is its geographical distribution outside the limits of New York City.

John W. D. Megaw

SHEPARD, C. C. **An Outbreak of Q Fever in a Chicago Packing House.** *Amer. J. Hyg.* 1947, Sept., v. 46, No. 2, 185–92, 2 figs. [10 refs.]

By complement-fixation tests a retrospective diagnosis of Q fever was made in connexion with a sharp outbreak of 33 cases of fever among 81 men engaged in slaughtering sheep and calves in a packing house in Chicago, during August, 1946.

The outbreak was similar in most respects to the one that occurred in Amalliro, Texas, in March 1946 [see this *Bulletin*, 1946, v. 43, 924]. There were no deaths. The original clinical diagnosis in most cases was pneumonia or influenza.

The patients had been engaged in handling and cutting up freshly killed animals and the highest attack rate was among those most exposed to splashing with blood and exudate from the carcases.

Droplet infection was regarded as the most likely mode of transmission of infection. There was no evidence of bites by ticks or other arthropods, and no cases occurred among workers who handled the animals before slaughter.

John W. D. Megaw

EKLUND, C. M., PARKER, R. R. & LACKMAN, D. B. **A Case of Q Fever probably contracted by Exposure to Ticks in Nature.** *Pub. Health Rep.* Wash. 1947, Sept. 26, v. 62, No. 39, 1413–16.

At the end of March 1947, a young man found himself infested by numerous ticks (*Dermacentor andersoni*) in the Bitterroot Mountains, Montana; he

crushed a number of the ticks with his fingers. Seventeen days later he became ill and suffered from headache and malaise for about 7 days.

Complement-fixation and rickettsia-agglutination tests for Q fever were negative on the 8th day, but on the 24th and 38th days both tests were positive. The titres observed with the former test were 1–128 to 1–512 against four different antigens, an Australian, two Italian, and " the original American " strain. The titre of complete agglutination of the Australian strain of rickettsiae was 1–40.

The authors state that the question arises whether infection could have been acquired through an abrasion of the skin, or even through the unbroken skin " as is the case in Rocky Mountain spotted fever." *John W. D. Megaw*

YELLOW FEVER

HOCKING, K. S. **The Use of Bamboo Pots to indicate *Aëdes* Prevalence.** *Bull. Entom. Res.* 1947, Aug., v. 38, Pt. 2, 327–33.

Various techniques have been used in attempts to estimate mosquito populations. With *Aëdes*, the commonest have consisted of counts of larvae or adults in houses, but these cannot be used in rural areas, *e.g.* around an aerodrome with no houses. The " Bamboo pot " technique gets over this difficulty. The " pots " consist of lengths of bamboo about 3 in. in internal diameter and one foot in length, filled with water and exposed in varying numbers and different localities, for periods of five days. Up to 75 per cent. were found to contain larvae in the experiments carried out. It is shown that this method of estimating *Aëdes* prevalence has fewer inaccuracies than those used previously, and it is particularly sensitive and valuable in well-controlled areas with few other breeding places. It can also be used in rural areas. *Kenneth Mellanby*

WADDELL, Mary B. & TAYLOR, R. M. **Studies on the Cyclic Passage of Yellow Fever Virus in South American Mammals and Mosquitoes. III. Further Observations on *Haemagogus equinus* as a Vector of the Virus.** *Amer. J. Trop. Med.* 1947, July, v. 27, No. 4, 471–6.

The authors first discuss the various factors which affect the chances of mosquitoes becoming infected with the yellow fever virus and their ability to transfer the infection to a susceptible vertebrate host. These factors have all been considered and investigated recently in previous papers by the authors and others working in South America [see especially this *Bulletin* throughout 1946]. They consider it virtually impossible to duplicate the conditions in any two transmission experiments and unless the conditions are the same results may vary irrespective of the vector employed.

In order to circumvent this contingency, in the experiments here reported, a vector chosen as a standard for comparison was introduced and submitted to the same conditions as the vector under study. The efficiency of the latter was then determined by comparing its transmission ratio with that of the standard vector.

First the alternate cyclic passage of yellow fever virus through *Haemagogus equinus* and *Callithrix aurita*, as described in a previous paper [see this *Bulletin*, 1946, v. 43, 33 ; 1947, v. 44, 309] was repeated for seven cycles. In this experiment, six to eighteen mosquitoes were allowed to feed each time.

A second experiment was carried out in which each individual mosquito was tested for virus. Infected marmosets were exposed at the same time to

normal *H. equinus* and *Aëdes aegypti*. Blood was removed from the marmosets immediately before the mosquitoes fed and was tested for virus content. The mosquitoes which imbibed blood were segregated and stored in an atmosphere having a temperature of 28–30°C. and humidity of 70 to 90 per cent. On 14th, 18th and 21st days thereafter they were permitted to feed individually on baby mice 2 to 3 days old. For each surviving *H. equinus* an *Aëdes aegypti* that had taken the infectious meal at the same time was tested. Though the number of mosquitoes tested was small, owing to high mortality of *H. equinus*, the ratio of transmission was higher with *Aëdes aegypti* irrespective of the length of incubation of the mosquitoes.

When the titre of circulating virus in the source marmoset was low at the time of feeding, few mosquitoes transmitted the infection. By this method of comparison against *Aëdes aegypti*, a ratio of transmission may be obtained which should serve for comparing one sylvan species with another.

F. O. MacCallum

DENGUE AND ALLIED FEVERS

FLEMING, R. F. & FRENCH, J. M. **Dengue in Iraq.** *Trans. Roy. Soc. Trop. Med. & Hyg.* **1947**, July, v. 40, No. 6, 851–60.

An account of an outbreak of febrile disease in a military hospital in Iraq in late 1944 among British, Indian and Arab troops. Of a total of over 60 cases, careful clinical and pathological investigations were carried out in 24 selected on account of lymphadenitis. The results of all pathological examinations, except for the presence of an almost constant leucopenia, were negative.

In the cases selected for special examination leucocyte counts varied from 8,200 to 4,000 per cmm. ; no absolute lymphocytosis suggestive of glandular fever was found, and Paul-Bunnell tests were negative. *Aëdes aegypti* were present in the neighbourhood. The patients usually had a sudden onset with chilliness but no rigors, the temperature rising to 104°F. ; severe headache, joint pains, backache and generalized aching were experienced. Severe occipital headache with pain and rigidity at the back of the neck in some cases suggested meningitis, but this was not confirmed.

The primary rash was macular or maculo-papular, appearing from the second day onwards, sometimes being so profuse as to suggest typhus ; while a secondary rash, when this was present, appeared on the last day of fever and was sometimes hard to detect. The majority showed neither primary nor secondary eruption. Bronchial symptoms with widespread rhonchi were often found ; the glands most commonly enlarged were the posterior cervical and epitrochlear groups. Bradycardia was almost always present.

Typical " saddle-back " temperatures were found in only three cases. The temperatures fell to normal on the 6th or 7th day, sometimes rising again to 99°–99·6°F. for a few days. Albuminuria was absent.

Laboratory examinations included numerous blood smears, total and differential leucocyte counts, blood cultures, agglutinations against the enteric and *Brucella* groups, Weil-Felix reactions, Wassermann and Kahn tests, examination for leptospirae. Diagnosis was made on the clinical course of the disease, the leucopenia, and the negative laboratory tests.

[The above, though not all typical " text-book " cases, certainly appear to have been dengue or some closely allied illness. There is a group of 6- or 7-day fevers, the manifestations of which seem to vary a good deal in different

outbreaks and localities. The reviewer, while in Iraq in 1920 and 1921, saw many cases of three-day (sandfly) fever but none clinically diagnosable as dengue.] *C. F. Shelton*

PLAGUE

SWELLENGREBEL, N. H. **Interhuman Transmission of Bubonic Plague.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Oct.–Nov.–Dec., v. 38, Nos. 10–11–12, 788–91. [French version 784–7.]

Interhuman transmission of bubonic plague reduces to a consideration of the efficiency in this respect of the human flea *Pulex irritans*. That it can become infected seems unquestionable, as also that it can remain infected for at least 21 days. Moreover, in North Africa, where this contention that plague may be transmitted by human fleas arises, infestation by these fleas is of such degree as is unknown in those parts of the world where flea transmission has been very thoroughly studied, India and Java. After consideration of all the arguments, Swellengrebel comes to the conclusion that " rat-fleas can be carried along in cargoes and by human beings without being accompanied by rats " and that antiplague measures must include disinsectization as well as deratization, together with control of human traffic. His final pronouncement is :— " Whatever the part *P. irritans* takes in plague transmission may ultimately prove to be, antimurine measures to prevent plague are highly specialised and directed against the murine population occupying human habitations only ; not, necessarily against other species, of rats, however important they may be from other points of view." *W. F. Harvey*

MANI. **Chemotherapy in Plague.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Oct.–Nov.–Dec., v. 58, Nos. 10–11–12, 800–807. [French version 792–9.]

Part I of this communication deals with chemotherapy and consists of abstracts of reports from 1940 onwards comparing the results obtained with sulphathiazole and sulphadiazine. The control used in comparison was iodine intravenously. Part II gives the use of a broth plague vaccine originally substituted for agar because of war difficulties. The broth vaccine, acid hydrolysate of casein of Muller and Johnson, has proved by mouse protection test to be as potent as the agar vaccine ; " is no more toxic and has the advantage of better keeping qualities." *W. F. Harvey*

CHOLERA

REIMANN, H. A. **Further Note on the Classification of Vibrios of the 1945 Cholera Epidemic in Chungking.** *Amer. J. Trop. Med.* 1947, July, v. 27, No. 4, 503.

Vibrios from several patients in the epidemic of cholera in Chungking in 1945 were classified as being of the Ogawa type in one laboratory [this *Bulletin*, 1947, v. 44, 423]. Dr. BURROWS of the University of Chicago examined the strains and reported different results. He has recently proposed a new classification of the cholera vibrio on a serological basis [*ibid.*, 422].

It would appear that, in cholera epidemics, either a single type strain or different serological types of the cholera vibrio are rampant. Questions arise

as to whether (*a*) epidemics begin from distribution of a single type and others appear as a result of bacterial dissociation or type transformation, or if epidemics are caused by one or more stable types of vibrio, and (*b*) if vibrios without antigen A—and presumably not cholera vibrios—may cause clinical cholera, or if they are dissociant culture phase forms of pathogenic vibrios brought about by extra-corporeal growth. *H. J. O'D. Burke-Gaffney*

YEN, C. H. **A Differential Medium for the Isolation of** *V. cholerae*. *Chinese Med. J.* Shanghai. 1947, May–June, v. 65, Nos. 5/6, 133–4.

In 1933, the author described a phenophthalein-starch medium for rapid isolation of *V. cholerae* [this *Bulletin*, 1934, v. 31, 44]. As this liquid medium rarely yielded pure cultures, although vibrion growth preponderated, he has modified it to a plate medium as follows :—

A mixture of 40 cc. egg-white, 280 cc. distilled water and 20 cc. *N*. NaOH is beaten thoroughly, boiled gently in a basin for 30 minutes and cooled to room temperature. There are then added 100 cc. of 10 per cent. aqueous solution of soluble starch, previously warmed to 40°C. and well shaken for 2 minutes. The volume is then made up to 1 litre with distilled water. To this are added :—

Peptone	10 gm.
Meat extract	3 gm.
Potassium nitrate ...	3 gm.
Sodium chloride	3 gm.
Maltose	1 gm.
Magnesium chloride ...	1 gm.
Agar agar	20 gm.

The mixture is heated, with frequent shaking in a waterbath for 1 hour, filtered through cotton and adjusted to *p*H 8·0. The filtrate is distributed in 100 cc. lots in flasks and autoclaved at 15 lb. pressure for 15 minutes. Just before plates are poured, 1 cc. of 1/10,000 malachite green in 95 per cent. alcohol and 0·5 cc. of 1/100 rosolic acid in 95 per cent. alcohol are added to each 100 cc. of medium and shaken until the indicators are evenly distributed. The medium is poured into plates to a depth of about 0·3 cm,. The surface of the cooled medium should not be excessively moist.

After 18 to 24 hours at 37°C., *V. cholerae* grows as transparent colonies with a clear greenish-yellow zone surrounding each one and standing out against the red background of the medium. This zone is due to the acid produced by the organism during fermentation of the starch. Various strains of common intestinal pathogens tested gave no such zone of discoloration. Staphylococci and enterococci were inhibited by the malachite green and rosolic acid. Mould contaminants could usually be distinguished morphologically and by their late appearance.

A total of 50 strains of *V. cholerae* gave the characteristic zone of decolorization but a laboratory strain of Inaba gave poor growth, owing to its sensitivity to rosolic acid ; nevertheless it showed the zone of decolorization. The medium has been found of great practical use for some years in isolating *V. cholerae*. *H. J. O'D. Burke-Gaffney*

HUANG, K. W. & MAO, Y. C. **Pa-Pin (Transient Paralysis) complicating Asiatic Cholera.** *Amer. J. Med. Sci.* 1947, Aug., v. 214, No. 2, 153–5. [12 refs.]

Pa-pin, which has been observed by the authors in 11 cases of cholera in the Chinese province of Szechuan, resembles the rare malady known as transient familial periodic paralysis. Clinical, laboratory and experimental work has pointed to barium poisoning as the cause of the malady. A further clue to the

nature of the paralysis is given in the curative action of this flaccid paralysis by administration of potassium. Although the condition is not familial in cholera nor yet a barium poisoning, it is reasonable to suppose that the pathogenesis is the same in both cases—a disturbance of potassium metabolism due to mobilization of barium from the bone reservoir as a result of dehydration and acidosis. In cholera the paralysis is late, " at the time of recovery from gastro-intestinal symptoms after several days salt-free diet, with no drugs except non-barium containing saline infusions." *W. F. Harvey*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

TRANS. ROY. SOC. TROP. MED. & HYG. 1947, Sept., v. 41, No. 1, 55–91. [35 refs.] **Discussion on Amoebiasis** [WENYON, C. M. (President); MURGATROYD, F.; MANSON-BAHR, P.; STEWART, G. T.; O'CONNOR, R. J.; MORTON, T. C.; GOODWIN, L. G.; NAPIER, L. E.; HOARE, C. A.; ANDREW, R. R.; STANNUS, H. S.; JONES, W. R.; COOKE, W. E.]

Dr. C. M. WENYON in his introductory remarks pointed out that interest in the subject of amoebiasis has been stimulated by great wars. This was the case during and after the 1914–1918 and also the 1939–1945 conflicts.

In the case of amoebiasis and other infections to which a large number of susceptible individuals are exposed, it is probable that the percentage of those who become infected is actually no greater than that which occurs in times of peace. The actual numbers are, however, much greater in war. It is probable also that most of the cases which appear refractory to emetine or other drugs eventually recover.

There are reasons for believing that epidemics of amoebic dysentery do not occur, and reference is made to the controversial instance of the Gallipoli outbreak in 1915 and the Chicago incident of 1933–1934.

It is strange that there is such little correlation between the incidence of healthy carriers and cases of amoebic dysentery. In the tropics, cases of amoebic dysentery are commoner than in colder countries and it is well understood that healthy persons, such as soldiers going overseas, amongst whom carriers occur, may develop amoebic dysentery soon after arrival in the tropics, when it is safe to assume they would not have done so if they had stayed at home.

If this is due to the original strain of *E. histolytica* then it denotes that some change in the intestinal mucosa must have taken place, possibly in the nature of the bacterial flora, as in the self-conducted experiments made by WESTPHAL. From observations on human beings and monkeys, it is clear that the extent of invasion of the intestinal mucosa varies considerably and that sometimes, as in monkeys, when there is no visible macroscopic lesion, examination of sections microscopically will reveal that some invasion has taken place. The question whether *E. histolytica* can live in the large intestine of man without giving rise to lesions, however minimal, cannot be answered. From his own experience Dr. Wenyon brought forward evidence that amoebic infection can be present without giving rise to any recognizable disturbance, and can then disappear without treatment.

A point of interest is the significance of the small race of *E. histolytica*. It is generally agreed that two races do occur. The question of behaviour of this race in the human intestine is difficult to decide as there do not appear to have been any satisfactory records of frank amoebic dysentery in man caused by it, so that we are left to surmise that the tendency to damage of the intestinal wall is less than in the large race.

As regards treatment of amoebic infections, Dr. Wenyon drew attention once more to his work with O'Connor in Egypt during the 1914–1918 war, when the best results were obtained by giving each morning for 12 days one grain injection of emetine subcutaneously, and half a grain in capsules each evening by mouth.

Dr. F. Murgatroyd dealt first with diagnosis. In intestinal amoebiasis, direct microscopic examination of freshly-passed stools remains the basic diagnostic procedure. He had been unable to confirm the provocative action of emetine in diagnosis, upon which so much has recently been written, and suggested that those who had found it of value should publish the data on which their findings rest.

In his experience, the value of sigmoidoscopy or proctoscopy is slight, nor is X-ray examination of much assistance in diagnosis. The complement-fixation reaction is neither readily applicable nor reliable.

Reviewing the various forms of antiamoebic treatment, he pointed out that until recently emetine hydrochloride and emetine bismuth iodide were much less used in the U.S.A. than in Great Britain, and that in the latter country diodoquin was virtually unknown. The initial promise of combined treatment with emetine bismuth iodide and chiniofon retention enemata had not been sustained. On the question of the possible part played by concomitant bacteria in the syndrome, he finds it difficult to believe that penicillin and sulphonamide can make much difference to the total results of treating amoebiasis, since, in general, the cases refractory to treatment are not necessarily those with gross lesions. Retention enemata of emetine 1 : 30,000 produce results no different from those obtained with chiniofon.

It is interesting that when an emetine enema is evacuated after some hours it shows no amoebicidal activity. Of 45 patients given chiniofon enemata, 31 appeared cured, 3 relapsed and the fate of 11 is unknown : of 53 given emetine enemata, 31 appeared cured, 5 relapsed and the results of 17 are unknown. It is suggested that the advantages gained by retention enemata in general are doubtful. To explain cases of amoebiasis refractory to treatment it is suggested that amoebae may vary in their resistance to the drugs employed, so that inadequate treatment may lead to drug resistance. Together with Goodwin, Dr. Murgatroyd has been able to bring forward evidence, by observations on infected rats, that emetine-resistance is indeed a reality. On drug metabolism we have little precise knowledge. In the case of emetine, the tests are insufficiently sensitive to follow the drug through the body. Speculations are based on therapeutic results. Thus the failure of emetine to cure amoebiasis in cats is attributed to rapid excretion in the urine. Save in a small percentage of human patients, emetine hydrochloride in doses of 1 grain daily appears either insufficient to maintain an amoebicidal medium in the tissues for a sufficient length of time to eradicate infection, or it fails to destroy the parasites in the lumen of the gut. This method, however, has been considered adequate by many in India.

The necessity of giving emetine bismuth iodide in a form in which it becomes dispersed in the gut is discussed. The addition of emetine hydrochloride parenterally in "loading" doses at the beginning of treatment with E.B.I. may be reasonable.

It seems reasonable also to treat asymptomatic carriers of *E. histolytica* whenever possible. Dr. Murgatroyd is convinced that many of the questions raised can be settled only by general agreement on the criteria for diagnosis and the necessity of further coordinated laboratory research.

Sir Philip Manson-Bahr described the advantages of diagnosis by proctoscopy together with the variable appearances observed.

He believed that the biopsy pictures obtained from the mucous membrane are diagnostically important.

Radioscopy is of little practical value, save in amoebic typhlitis, where a peculiar filling defect of the caecum may sometimes be of decisive diagnostic value.

Dr. G. T. STEWART described added bacterial infection in amoebiasis and post-dysenteric colitis. The problem of intestinal amoebiasis is twofold. Firstly there is straightforward amoebic infection and secondly the possibility of further infection by bacteria. Post-dysenteric colitis should be kept apart from the psychosomatic disorders which are grouped under " irritable colon ".

The main qualitative alterations in the bacterial flora of the faeces in cases of diarrhoea due to active amoebiasis and post-dysenteric colitis are given in a table and compared with control cases. *Bact. coli* is equally prevalent in both groups, whilst paracolon bacilli and *Streptococcus faecalis* are more prevalent in the dysenteric group, and statistical analysis suggests that the increased prevalence is unlikely to have arisen by chance.

In vitro penicillin inhibits strains of *Bact. coli*, paracolon bacilli and *S. faecalis* at concentrations ranging from 20 to 100 units per cc., but in the presence of certain sulphonamides a synergic action obtains whereby the effective bacteriostatic concentration of each drug is lowered. On this evidence, Dr. Stewart has given penicillin parenterally, with sulphathiazole orally, to some patients and penicillin rectally to others.

Dr. R. J. O'CONNOR has investigated the fate of penicillin administered rectally in treatment of amoebiasis. It was found that the first motion passed contained a large amount of penicillin at a high concentration, but subsequent motions contained little or none. The results obtained were sufficiently constant to suggest that by the rectal administration of penicillin, urinary levels of some therapeutic value might be obtained.

Air-Commodore MORTON described acute fulminating amoebic dysentery, an amoeboma simulating a neoplasm, amoebic abscess of the liver, heralded by generalized urticaria, and amoebic typhlitis simulating appendicitis, with an *Ascaris* impacted in the appendix. He also outlined a course of treatment which had been found invaluable in very chronic relapsing cases. It consists of penicillin 1·5 mega units by needle+100 gm. of sulphasuccidine for the first 5 days, followed by 1 grain of emetine for 6–10 days, the latter dosage being reserved for cases in which there is a leucocytosis ; together with the emetine, the patient received 3 tablets t.d.s. of diodoquin for 21 days. This is followed by emetine enseals (Eli Lilly & Co.) 2 tablets of $\frac{1}{3}$ grain each t.d.s. for 10 days, together with chiniofon retention enema of $2\frac{1}{2}$ per cent., commencing with 250 cc. and going up to 700 cc. This has proved effective in every one of his resistant war cases up to date. It has been proved conclusively, by barium enema of the same consistency, that with 200 cc. the splenic flexure is reached, with 500 cc. the hepatic flexure, and with 700 cc. the caecum.

Mr. L. G. GOODWIN showed a film recording a method of producing experimental infections with *E. histolytica* in young rats. The methods developed at the Wellcome Laboratories differ somewhat from those described by W. R. JONES [this *Bulletin*, 1947, v. 44, 313]. It has been shown that strains derived from different sources vary in their infectivity for the rat and that pathogenicity does not depend upon the number of amoebae injected, nor upon the severity of the human infections from which they were derived. It has been shown that a strain from a symptomless carrier will produce severe lesions in the rats' caecum.

Dr. C. A. HOARE spoke on certain aspects of the host-parasite relationship in amoebiasis, particularly with the mode of life of *Entamoeba histolytica* in the human host. He had been able to convince himself that a certain proportion

of amoebae from cases of chronic amoebiasis have food vacuoles containing bacteria. In natural and experimental infection of macaque monkeys, *E. histolytica* behaves in most cases as a true commensal, living in the lumen of the gut and feeding on bacteria and foecal débris ; and in experimentally infected rats the amoebae live as commensals, ingest bacteria, invade the intestinal wall and feed on red blood corpuscles.

The views of some authors that the amoebae living in the lumen of the gut are the only forms capable of encysting and propagating the infection need verification, whilst others have found that these forms are more resistant to the action of emetine than the tissue forms. *P. Manson-Bahr*

NAPIER, L. E. **The Cyst-Passer.** *J. Trop. Med. & Hyg.* 1947, Sept., v. 50, No. 9, 169–74.

In an editorial article Napier discusses the significance of *Entamoeba histolytica* infections in " cyst passers." Some hold that such carriers, like diphtheria and typhoid carriers, are a menace to the community ; others consider their infections invariably pathogenic, and so incompatible to perfect health in the individual ; a third group regards the infection as only doubtfully pathogenic, and so common that little can be done about it in practice ; and a fourth believes the infection of no clinical significance if unattended by physical signs or symptoms. Stool surveys show very high rates (55·5 per cent.) of infection in certain communities in the temperate and subtropical zones ; and in England, some years ago, 11 per cent. of a cross section of the population was found to be infected. A person may pass cysts for a year or two and then cease to do so ; so the current infection-rates do not necessarily indicate the true incidence of infection in a population.

As amoebic dysentery [as opposed to amoebiasis] is essentially a tropical disease it is difficult to believe that pathological lesions are present in every case of infestation with *E. histolytica*, and the evidence in support of this contention is conflicting. *E. histolytica* can be cultured in the absence of mammalian cells, and so may live commensally in the gut of man. The theories put forward to account for its penetration into tissues include (1) variations between strains of parasites ; (2) the need for a synergistic bacterial or virus infection ; or (3) differences in the resistance or degree of immunity of individual hosts. Arguments for and against these are considered at some length, but none of them has been substantiated ; these matters require reinvestigation.

If there is sound evidence that infection with *E. histolytica* invariably is associated with penetration of the gut tissues, routine examination of at least all sick persons in temperate climates should be done to exclude amoebiasis, and those infected should be treated ; furthermore, cyst passers in the temperate climates should be sought out and their infections eradicated in the interests of public health. The author considers it irrational to ignore the millions passing cysts in the temperate climates, while treating rigorously those few symptom-free individuals in whom the infection has casually been discovered. The convalescent cyst passer in or from the tropics he holds to constitute an entirely different problem. *A. R. D. Adams*

REES, C. W., REARDON, Lucy V., JONES, Frances E. & GRIFFIN, A. M., with the technical assistance of Ida L. BARTGIS. **Observations on the Excystation of** *Endamoeba histolytica*. *J. Parasitology*. 1947, Aug., v. 33, No. 4, 385.

The senior author (*Amer. J. Trop. Med.*, 1942, v. 22, 487) reported a micro-isolation technique for obtaining bacteria-free cysts of *Entamoeba histolytica*

which provided cultures of the amoebae with selected single species of bacteria: no cultures were produced by the cysts in the absence of bacteria. It could not be ascertained with this technique whether excystation occurred in bacteria-free preparations, as negative results were always obtained.

The technique has therefore been modified so that the cysts may be isolated in microculture tubes through the walls of which the organisms can be seen microscopically throughout the experiment. These culture tubes are made from capillary glass tubing in which appropriate media are placed; the cysts were observed by immersion of the sealed tubes in water. In microcultures prepared without bacteria, excystation was seen in all media except Locke's solution, suggesting that some substances in the media facilitated excystation and that dextrose alone was inadequate for this purpose. In examination of 800 microcultures containing some 7,000 cysts, 17 per cent. were found to excyst in one series, but less than 1 per cent. in others. The rates of excystation were surprisingly low (25 to 75 per cent. of cysts were tetranucleate). Rates of excystation did not vary as between cysts from human stools or those from culture, nor were they affected significantly by the addition of cysteine hydrochloride to the media. Since control cultures only showed slightly higher rates of excystation than did bacteria-free cultures, it would appear that the growth of bacteria may not have provided optimum conditions for excystation. Comparable results were obtained with *Entamoeba coli*.

H. J. O'D. Burke-Gaffney

JACOBS, L. **The Elimination of Viable Bacteria from Cultures of** *Endamoeba histolytica* **and the Subsequent Maintenance of such Cultures.** *Amer. J. Hyg.* 1947, Sept., v. 46, No. 2, 172–6.

The medium employed consisted of the usual egg-slant-Locke's solution conditioned by the cultivation in it for 24 hours of *Bact. coli* followed by killing of the bacteria by heat. After heating, rice powder and heat-killed *Bact. coli* or *Staphylococcus aureus* were added. Tubes of this conditioned medium with and without penicillin (100–200 units per cc.) and unconditioned medium were set up. The tubes were inoculated with 0·5 cc. of amoebic culture. Examination of the tubes for bacteria and amoebae were carried out at 24, 48 and 72 hours. The control tubes of unconditioned medium with penicillin were always negative for amoebae. By sub-culture from positive tubes, amoebae were grown in two instances for 3·5 months and 2·5 months. For some reason which is not clear the first strain ceased to grow but the second is still being maintained. Exhaustive bacterial tests have failed to demonstrate any living organisms upon which the amoebae might have fed. [See also this *Bulletin*, 1947, v. 44, 582; 661.]

C. M. Wenyon

BRACKETT, S. & BLIZNICK, A. **The Rate of Multiplication of** *Endamoeba histolytica* **and its relation to** *in vitro* **Drug Testing and possibly to Nutritional Studies.** *J. Parasitology.* 1947, Apr., v. 33, No. 2, 154–66. [35 refs.]

With cultures of *E. histolytica* grown in association with the "t" organism [this *Bulletin*, 1943, v. 40, 456] in egg-slope covered with Locke's solution to which rice starch was added, tests have been made on a number of substances which had been tried for anti-malarial activity. Inocula varied from 1,500 to 5,000 amoebae, but as few as 15 amoebae frequently gave positive cultures. The maximum increase in amoebae seen in a single transfer was 36,000 times or about 15 generations. The average number of divisions per day was from two to two and a half. The substances tested were dissolved in the liquid of the medium. Vioform and emetine were amoebastatic in strengths of

1: 200,000. Other compounds which were inhibitory at about the same level were para-aminobenzoic acid, 2-n-hepatyl-4, 6-diamino-s-triazine and 2-methyl-4-amino-5-bromomethylpyrimidine. These substances act directly on the amoebae; they did not inhibit growth of the "t" organism. Sulphadiazine and related substances inhibit the amoebae, though indirectly, through their action on the "t" organism. Metachloridine, paludrine and plasmoquine are only active at high concentrations. *C. M. Wenyon*

ALKAN, W. J. **Amoebiasis, Diagnostic and Therapeutic Considerations.** *J. Trop. Med. & Hyg.* 1947, Sept., v. 50, No. 9, 175–82, 3 figs. [13 refs.]

This work was carried out chiefly in an Indian General Hospital (Combined) working in Greece and Italy and dealing mainly with Indian patients. Out of 4,995 cases treated, amoebiasis was diagnosed in 66, *viz.*, dysenteric 32; hepatitis 17; liver abscess 1; cutaneous 2; cyst passers 14. Of all the dysenteries, 20 per cent. were amoebic, and of all diarrhoeic and dysenteric conditions 11 per cent. were amoebic.

The author found that "typical cases" of amoebic dysentery were comparatively rare, and that more often the patients had vague dyspeptic symptoms accompanied by loss of weight and energy. Many gave a history of passing loose motions for a few days, followed by a brief period of constipation with small hard faeces. On clinical examination a moderate tenderness over the caecum or sigmoid was often found.

The following method is recommended to establish a definite diagnosis in suspected cases. Three fresh warm stools, free from urine or antiseptics, are examined; if no *E. histolytica* are found the parasite may be detected in stools passed after giving a saturated solution of 1 oz. of magnesium sulphate before breakfast. [It is suggested that ideally the microscope should be taken to the bedside or commode and the specimen examined immediately after it has been passed.] If these investigations are negative, a concentration method for cysts may be tried; and if the stools are persistently negative, sigmoidoscopy preceded by digital examination of the rectum should be performed. The possible co-existence of malignant disease with amoebiasis should always be kept in mind and two cases, one of rectal carcinoma and the other of carcinoma of the hepatic flexure, are described. Both had previously been diagnosed as amoebiasis, and had shown only temporary improvement under treatment—in the latter, *E. histolytica* was eventually found. If all examinations are negative, a therapeutic test is indicated in suspect cases; and even in proved cases of amoebiasis which do not respond to treatment, a barium enema should be given to exclude growths of the colon. The possibility of co-existence of a new growth and a parasitic infection should always be kept in mind, especially when the latter is only found during the later stages of a chronic condition.

Symptoms suggestive of appendicitis may cause difficulty in diagnosis, and the following course is recommended in such cases:—

1. Where amoebiasis is endemic, or where there is a history suggestive of such, at least one fresh stool is examined.

2. If there is microscopic or clinical evidence of amoebiasis, emetine should be given and the case most carefully watched, laparotomy being indicated if the acute condition persists.

In supposed cases of ulcerative colitis, even if *E. histolytica* cannot be found, emetine should be tried; of course, bacillary and amoebic dysentery may coincide.

Dealing with complications the author states that the clinical course of liver abscess was typical; amoebic hepatitis was often atypical, with low-grade pyrexia and often normal or slightly raised leucocyte counts, while many cases diagnosed as "right pleural effusion" turned out to be hepatitis and responding to emetine. Two cases of perianal cutaneous amoebiasis [this must be a rare condition], confirmed microscopically, responded well to the usual anti-amoebic treatment. An interesting sequela of chronic caecal amoebiasis was found to be intestinal mal-absorption with steatorrhoea.

Treatment.—Emetine has an immediate effect in most acute infections, but when given alone it will not bring about a cure in most cases. It has no effect on cysts, but appears to be a specific in hepatitis. Emetine-resistant strains are possibly produced by indiscriminate use of this drug and its administration in insufficient doses.

Failure of Treatment.—This may be due to :—

1. Insufficient treatment: Emetine requires to be supplemented by some other drug, *e.g.*, carbarsone.

2. Faulty technique: E.B.I. may be passed unabsorbed, owing to an insoluble coating in certain preparations; the stools should become a blackish colour during treatment with this drug.

3. Retention enemas (quinoxyl, yatren, etc.) containing about 2½ to 4 per cent. of the preparation, should be preceded by a wash out of about half a pint of two per cent. sodium bicarbonate solution and should consist of not more than 300 ml., given preferably by the drip method. The patient lies on his back for half an hour, then on the left side for half an hour, again on the back for the same period, and then on the right side for half an hour. For the remainder of the treatment (5 to 7 hours) he lies on his back.

4. Diet: A well-balanced diet, with a minimum of roughage, and no alcohol should be given. In the past, patients have sometimes been underfed.

5. Undiagnosed co-existing conditions, *e.g.*, bacillary dysentery, *Giardia* and *Trichomonas* infections, malaria, kala azar.

However, after elimination of all possible fallacies, a proportion of patients relapse despite all treatment.

Indiscriminate repetition of periodic courses of emetine is to be deprecated and may be dangerous; it may also possibly produce emetine-fast strains of *E. histolytica.*

"Apacol," the Chinese "Ya Tan Tzu," diodoquin (containing 60 per cent. iodine) have all been claimed to have had successes.

Follow-up Procedure.—

1. Examination of at least 6 stools, three after administration of magnesium sulphate. Sigmoidoscopy and microscopic examination of specimens taken directly from suspicious areas.

2. Stool examinations as (1) after one month. Sigmoidoscopy if indicated.

3. Stool and general examination three months after stoppage of treatment.

[On page 180 the statement is made that emetine is made ineffective by heat sterilization. Many authorities will not agree with this observation.]

C. F. Shelton

PARKINSON, T. **Amoebiasis in Ceylon.** *Lancet.* 1947, Oct. 25, 612–15.

The object of this paper is to show how high is the incidence of amoebiasis in Ceylon.

The total admissions to the medical wards of an R.A.F. mobile field hospital between October 1944 and September 1945 were 635: of these 191 were for dysenteric disorders, as shown :—

Amoebic group		97	(50·8 per cent.)
Primary acute amoebic dysentery ...	62		
Acute relapse of amoebic dysentery ...	9		
Chronic intestinal amoebiasis	15		
Amoebic hepatitis	9		
Liver abscess	2		
Bacillary Dysentery		15	(7·9 per cent.)
Clinical dysentery		14	(7·3 per cent.)
Non-specific diarrhoea		63	(32·9 per cent.)
Lambliasis		2	(1·1 per cent.)

The reason for the relatively low incidence of bacillary dysentery is attributed to the fact that there was no epidemic, probably because the fly menace was avoided by DDT and the high standard of hygiene.

It is claimed that half the patients admitted to hospital with diarrhoea had amoebic dysentery.

The efficacy of sulphonamides in the treatment of bacillary dysentery is such that it became customary to use these drugs as a therapeutic diagnostic test ; but this approach is fallacious, as the author's observations on selected cases show that sulphonamides at least mask the symptoms of acute amoebiasis and may have some amoebicidal action. It is suggested that secondary bacterial infection of the bowel may precipitate an acute attack of amoebic dysentery and be responsible for chronicity of other cases ; but the rapid disappearance of *E. histolytica* from the stools in 5 cases suggests that these drugs are lethal to the amoebae. Thereafter it was customary to use a short course of chemotherapy together with emetine as initial treatment in acute amoebiasis. The following course was adopted :—

Days 1–10 ...	Emetine 1 grain
Days 1–3 ...	Sulphapyridine (or sulphathiazole) total 14–20 gm.
Days 4–13 ...	Carbarsone 4 grains b.d.
Days 14–20 ...	Rest
Days 21–30 ...	E.B.I. 1–3 grains nightly (according to tolerance).

Forty-two patients with acute amoebiasis were treated on these lines. Of these it was possible to follow up 15 at an interval of 2 to 4 months after discharge from hospital. The results, both immediate and remote, have been impressive.

It is generally accepted that a leucocytosis is a distinctive feature of amoebic hepatitis, but only 5 out of 10 patients with this condition had a count of over 10,000 and others showed a moderate leucopenia. Only 6 gave a previous history of diarrhoea and in 5 of the 10 no *E. histolytica* or cysts were found in the stools. *P. Manson-Bahr*

LEBON, J., MAIRE, R., DUBOUCHER, G. & CLAUDE, R. Amibiase intestinale récidivante traitée par l'association pénicilline, sulfaguanidine et émétine. [**Relapsing Amoebic Dysentery treated with a Combination of Penicillin, Sulphaguanidine and Emetine.**] *Algérie Méd.* 1947, Aug.–Sept., No. 7, 562–4.

Account of a case.

MANSON-BAHR, P. **Amoebic Abscess of the Spleen.** *J. Trop. Med. & Hyg.* 1947, Sept., v. 50, No. 9, 174–5.

Generally speaking, abscesses of the spleen are extremely rare, and when they occur they are usually associated with bacterial infections.

Amoebic abscess of the spleen is of extreme rarity, and the author has been able to find but a few references to it in the literature, although most text books

refer to it. Among others, MAXWELL (*The Diseases of China*, 1929, Shanghai), describes six cases in Formosa, and FRANK [this *Bulletin*, 1944, v. 41, 572] describes one in an Indian girl.

In December 1946, the present author saw an officer from Burma, who had been invalided a year previously, after 20 years' service, during the last 11 of which he had suffered from a marked splenomegaly, believed to be malarial in origin. In 1942, in Burma, he began to suffer from increasing splenic pain. On his return to England, an abscess commenced to point in the abdominal wall in the left hypochrondrium ; this was opened and the sinus healed spontaneously. In November 1946, the sinus reopened and discharged "anchovy-sauce" material. The spleen edge was hard and extended 4 inches below the costal margin ; the sinus was found to extend 2½ inches towards the centre of the spleen. The patient was generally in good condition, without fever.

Microscopically, the discharge closely resembled "liver pus", but no *Entamoeba histolytica* were found in it, nor were cysts demonstrated in the stools : there was a leucocytosis of 10,800 per cmm. X-ray examination showed slight enlargement of the liver shadow and some elevation of the diaphragmatic dome. The left lobe of the liver was not obviously altered. No connexion with the spleen was demonstrated by lipiodol injection of the sinus. a few streptococci were found in the pus from the sinus, but penicillin injections were without effect.

Emetine injections were given and the sinus began to diminish ; simultaneously, the bulk of the spleen became progressively smaller on emetine bismuth iodide ; within a month the spleen was no longer palpable. The patient remains in excellent health.

While the aetiological agent was not demonstrated, the history and the rapid response of the abscess to anti-amoebic therapy seem to provide conclusive evidence that this was a genuine example of an amoebic abscess of the spleen.

H. J. O'D. Burke-Gaffney

SHUN-SHIN, M. **Balantidial Dysentery in Rodriguez and its Treatment with Mercury Biniodide.** *Brit. Med. J.* 1947, Sept. 13, 417–18.

The paper describes ten cases of balantidial dysentery in Rodriguez, an island 350 miles from Mauritius. Seven of the cases were in children from 3 to 13 years of age, and three were in adults 30, 40 and 63 years of age. One patient, a man aged 30, was treated with mepacrine and a mixture of bismuth and opium. His condition did not improve and he died five days later. All the other patients were treated with biniodide of mercury (1/24 to ½ grain) administered intramuscularly. Two or more injections were given and in all cases a cure was obtained. The island is 40 square miles and has a population of 12,000. Every household breeds at least one pig and as the hygienic conditions are unsatisfactory, balantidial dysentery is to be expected. *C. M. Wenyon*

TOMPKINS, V. N. & MILLER, J. K. **Staining Intestinal Protozoa with Iron-Hematoxylin-Phosphotungstic Acid.** *Amer. J. Clin. Path.* 1947, v. 17, 755–8. [Abstract by the authors.]

'A modification of Heidenhain's iron-hematoxylin method of staining intestinal protozoa is presented. The basic change is the application of 2 per cent. phosphotungstic acid for differentiation. This differentiator is automatic and

self-limiting requiring no microscopic control. Uniform permanent film preparations of fecal specimens may be obtained rapidly by the modified procedure even by persons of limited experience."

RELAPSING FEVER AND OTHER SPIROCHAETOSES

KAMAL, A. M., ANWAR, M., ABDEL MESSIH, G. & KOLTA, Z. **Louse-borne Relapsing Fever in Egypt. A Review of 9,977 Cases.** *J. Egyptian Pub. Health Ass.* 1947, Jan., v. 22, No. 1, 1–22, 1 chart.

The authors attempt to summarize the history of louse-borne relapsing fever in Egypt, which was first definitely recorded in the country by Sandwith and Engel in 1884, although it was probably seen by the doctors accompanying Napoleon when he invaded Egypt.

The yearly incidence of the disease from 1906 to 1946 is given in tabular form. For the first ten years, a few hundred cases occurred in most years and then from 1916 to 1920 there was an epidemic involving nearly 40,000 cases, after which the incidence rapidly declined and only 8 cases were recorded between 1926 and October 1944. At the end of 1944, there were 10 cases, in 1945, 18,277, and in 1946 up to September, 108,882 cases, with 2,367 deaths. This great epidemic started in the Beni-Suef Province, and during 1945 spread to every part of the country except Aswan and Damietta. In April 1946, the number of cases reached its peak, after which it declined, and during the week ending September 30th only 25 cases were recorded.

The authors compare the incidence of relapsing fever with that of the other prevalent louse-borne disease—typhus—and remark that this infection spreads more readily than relapsing fever among the inhabitants of the Delta. Moreover, typhus remains endemic in the country, whilst relapsing fever disappears after each epidemic. Of 9,977 cases, 6,596 were males and 3,381 females.

A total of 3,011 cases were treated with one injection of arsphenamine. The dose for adults was 0·60 gm. given intravenously, and for children the dose was reduced according to age. Of these 3,011 treated cases, 623 relapsed, whilst of 1,623 untreated cases, 1,182 relapsed. Most of the relapses occurred before the 11th day of convalescence and the authors consider that patients should not be discharged until after 14 days' apyrexia from the first attack.

A group of 365 cases was treated with two doses of arsphenamine on two consecutive days, and 39 relapsed. Mapharside, injected for three consecutive days, was used for 371 cases and gave 27 relapses; but apart from the disadvantage of delaying the appearance of these relapses, there were other objections to its use, as it was very painful on injection, and induced rigors and vomiting.

The effect of treatment on the case fatality rate is indicated in the following table :—

	No. of cases	Fatality rate per cent.
Untreated	245	4·5
Treated—Arsphenamine (1 inj.) ...	180	3·3
,, (2 inj.) ...	107	1·9
Mapharside	124	0·9

E. Hindle

GARNHAM, P. C. C., DAVIES, C. W., HEISCH, R. B. & TIMMS, G. L. **An Epidemic of Louse-borne Relapsing Fever in Kenya.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Sept., v. 41, No. 1, 141–70, 9 figs. (2 on 1 pl.) [37 refs.]

An interesting account of the first epidemic of louse-borne relapsing fever to have been recorded in East Africa. [This disease, however, is well known in Abyssinia and the Sudan.]

The epidemic was introduced into Kenya from South Arabia in February 1945, when a number of Arab dhows arrived at Mombasa with cases on board. It gradually spread and by October had reached epidemic proportions. In all there were about 2,000 cases in a population of 110,000 and the mortality in untreated cases was 40 per cent.

Various control measures, including the disinfestation of about 100,000 people by dusting with 5 per cent. DDT powder, rapidly terminated the epidemic.

The clinical features were fairly typical, but the cases were characterized by the prominence of neurological symptoms, cardiac involvement, positive Weil-Felix and negative Kahn reactions. Blood examined during the initial attack nearly always showed spirochaetes, but during relapses they were often absent or very scanty.

Lice collected from patients with spirochaetes in their blood were examined both microscopically and by inoculation into animals, but gave uniformly negative results. Subsequently, lice were kept alive for 13 days after being collected; in these spirochaetes were found in large numbers, and infection was produced by inoculation into monkeys. No *Ornithodorus* was ever found, and bugs collected from infected huts were negative. Attempts were made, without success, to transmit the infection by *Ornithodorus moubata* and *O. savignyi*.

Rabbits, guineapigs, bush-babies (*Galago crassicaudatus*) white rats, white mice, gerbilles and 5 species of African monkeys, were infected experimentally, and showed this order of susceptibility, rabbits being the least and monkeys the most susceptible. Repeated passage in mice was easily maintained; neurotropism hardly ever occurred.

The infections in lice showed a well-marked negative phase lasting till the 16th day; and lice collected from patients and examined within 24 hours never showed spirochaetes. In view of the different results recorded in Abyssinia and China, it is suggested that louse-borne spirochaetes may be divided into two groups: the first with a long negative phase in the louse, including the European, North African and Abyssinian strains, and the second without this phase, spirochaetes being continually present throughout the louse cycle, as in the Abyssinian and Chinese strains.

No cross immunity could be detected between *S. recurrentis* and *S. duttoni* in mice and rats, but a relatively refractory bush-baby was immune to *S. duttoni* after recovery from *S. recurrentis*.

Auto-agglutination of spirochaetes in old infections occurred in monkeys but not in rats. The pathogenicity of the Kenya strain in man and animals was found to resemble most closely that of *S. carteri* and differed markedly from the Chinese and Abyssinian strains. The pathological changes resembled those previously described except that in three cases degeneration of ganglion cells was found in the cerebellum without meningo-vascular inflammation.

E. Hindle.

SINGER, J. Considerațiuni hematologice in diagnosticul febrei recurente. [**Haematological Factors in the Diagnosis of Relapsing Fever.**] *Rev. Științelor Med.* Bucharest. 1947, Jan.–Apr., v. 36, Nos. 1/4, 96–108, 6 figs. on 2 pls. French summary.

TOPCIU, V. Frecvenţa complicatiilor pleuro-pulmonare in cursul febrei recurente. [**The Frequency of Pleuro-Pneumonic Complications in Relapsing Fever.**] *Rev. Ştiinţelor Med.* Bucharest. 1947, Jan.–Apr., v. 36, Nos. 1/4, 129–31.

The complication was found in 18 per cent. of 150 patients.

YAWS

LOPES, C. F. Contribuição ao estudo da lesão primária da bouba. Nota prévia. [**A Preliminary Note on the Primary Lesion of Yaws.**] *Hospital.* Rio de Janeiro. 1945, Dec., v. 28, No. 6, 987–97, 9 figs. English summary.

The author believes that the primary lesion of yaws may be distinguished readily from the secondary. It is usually larger, flatter, situated below the knees, and causes a definite lymph gland reaction : the affected gland is slightly painful, may enlarge to the size of a pigeon's egg, but does not suppurate.

The author considers one feature to be characteristic of the primary lesion : this is a whitish areola around the lesion, in which the skin is dry, rough, keratotic and furfuraceous. This areola is of variable size, may be circinate, and is seen on only one side of the lesion, " like a diadem".

He has seen this areola in about one-third of his patients with the primary lesion, but never in the secondary. The histopathological study of this feature will be the subject of another publication.

The paper is illustrated with nine photographs of lesions.

H. J. O'D. Burke-Gaffney

DWINELLE, J. H., SHELDON, A. J., REIN, C. R. & STERNBERG, T. H. **Evaluation of Penicillin in the Treatment of Yaws. Final Report.** *Amer. J. Trop. Med.* 1947, Sept., v. 27, No. 5, 633–41.

The authors report observations made up to 12 months after treatment with penicillin of 500 cases of primary and secondary yaws in Haiti. The schedules were : 1,200,000 units of penicillin sodium in water intramuscularly in 4 days (Series A) ; the same total dosage of penicillin in arachis oil and 4·8 per cent. beeswax (300,000 units of penicillin calcium per cc.) in two injections, 24 hours apart (Series B) ; and the same schedule as B, but 10–12 hours apart (Series C). In series B and C, dosages for children were graded down. The preliminary report has been reviewed in this *Bulletin*, 1946, v. 43, 1043, where the composition of the series treated was tabulated. No severe reactions were observed, but about half of the patients in Series A had pyrexia up to 100–104°F. (37·5–40°C.), coming on 2–8 hours after treatment started, and lasting 10–12 hours.

Results were grouped under the following headings :— " Apparent cure," with clinical cure and persistent negative Kahn tests ; " Satisfactory progress," with clinical cure but progressive reduction of Kahn titre to a persistent low level, but never becoming negative ; and " Unsatisfactory progress " which included " reinfections," " clinical relapse " and " serological relapse."

Patients in Series A were observed every month and those in Series B and C at intervals of 3 months. The results are shown in the following table, taken from the article :—

Primary and Secondary Yaws treated with 1,200,000 *units Penicillin intramuscularly.*

Series A 30,000 units in water 3-hourly for 4 days	Period of observation in months				Total Number of patients	Percent. of total
	0–3	4–6	7–9	10–12		
" Apparent cure " (1) ...	0	0	5	47	52	26·7
" Satisfactory progress " (2)...	5	5	7	106	123	63·5
(1)+(2)	5	5	12	153	175	90·2
" Unsatisfactory progress " ...	0	1	3	15	19	9·8
Total ...	5	6	15	168	194	
Series B In arachis oil and beeswax in 2 doses 24 hours apart	3	6	9	12		
" Apparent cure " (1) ...	0	1	3	10	14	11·0
" Satisfactory progress " (2)...	14	8	17	65	104	81·9
(1)+(2)	14	9	20	75	118	92·9
" Unsatisfactory progress " ...	0	1	5	3	9	7·1
Total ...	14	10	25	78	127	
Series C In arachis oil and beeswax in 2 doses 10–12 hours apart	3	6	9	12		
" Apparent cure " (1) ...	0	0	1	7	8	6·4
" Satisfactory progress " (2)...	13	10	23	62	108	86·4
(1)+(2)	13	10	24	69	116	92·8
" Unsatisfactory progress " ...	1	1	2	5	9	7·2
Total ...	14	11	26	74	125	

The higher percentage (26·7) of serological (" apparent cure ") cases in Series A after 12 months may be due to the longer course (4 days) of treatment or to a change in the composition of penicillin which occurred in 1945, between the treatment of Series A and Series B and C. This is balanced by the higher percentage of " satisfactory progress " cases in Series B and C, so that the percentages of " Apparent cure " and " Satisfactory progress " together in each Series is approximately the same, *i.e.* 90–93. Since, in Series A, children received the same dose as adults with no difference in serological response from them, it is suggested " that the amount of penicillin beyond a certain minimum was not the essential factor in producing serological reversals." Duration of infection also apparently had no effect on the response to penicillin.

Of the " Unsatisfactory progress " cases (8·3 per cent.) at the end of 12 months, in Series A, B and C respectively, " Reinfection " had occurred in 3·1, 1·6 and 2·4 per cent., " Clinical relapses " in 0, 2·4 and 0·8 per cent. and " Serological relapses " in 6·7, 3·1 and 4·0 per cent. Surprisingly few patients

were reinfected, 2 per cent. of all the series combined ; in about half of these, the Kahn titre had increased 1–2 months before the " Reinfection." Only 0·9 per cent. of the series combined were " Clinical relapses." " Serological relapses " comprised 4·9 per cent.

The authors regard penicillin as the present-day drug of choice in the treatment of yaws, particularly the arachis oil and beeswax preparation, because of the short course needed and the great reduction in cases of reinfection. It should rapidly bring yaws under control.

[Even if half the " Reinfections " are included in the " Clinical relapses," their low incidence suggests that the low Kahn titres of the " satisfactory progress " cases might, for practical purposes, be regarded as negatives. As the authors observe, longer observation might support this.]

C. J. Hackett

TURNER, T. B., MCLEOD, Charlotte & UPDYKE Elaine L. **Cross Immunity in Experimental Syphilis, Yaws, and Venereal Spirochetosis of Rabbits.** *Amer. J. Hyg.* 1947, Sept., v. 46, No. 2, 287–95.

Batches of 10–20 rabbits were inoculated intra-testicularly with *Treponema pallidum* (syphilis), *Trep. pertenue* (yaws) and *Trep. cuniculi* (venereal spirochaetosis of rabbits) respectively. Six months later they were inoculated intracutaneously with different strains of the same three species of treponema so that all possible cross-immunities could be observed. Results were compared with controls. Observations were made 21 and 35 days after the second inoculations. The tables show that there was considerable cross-immunity between all three species, perhaps less between syphilis or yaws and *cuniculi* infection than between yaws and syphilis. The protection of one infection against another is probably greater than the figures indicate, since the challenge doses were many thousands of times larger than those probably necessary to cause infection in unprotected rabbits.

It is pointed out that, in experimental syphilis, immunity is of three grades, permitting ; (*a*) symptomatic reinfection ; (*b*) asymptomatic reinfection ; or (*c*) no reinfection. It depends in part upon the resistance which the host has already developed and also upon the size of the challenge dose. Although it would be unwise to carry the results of experimental work on animals into the epidemiology of yaws and syphilis in man " nevertheless, the experimental results are entirely consistent with the other evidence of a clinical, epidemiological and experimental nature, which indicates that a serviceable degree of reciprocal immunity exists between yaws and syphilis as they occur in nature." Although there is little information regarding the minimal infective doses of yaws and syphilitic treponemata for man, under natural conditions doses would probably be small so that a relatively low immunity might often protect.

An anti-yaws and anti-syphilis measure in man worthy of closer investigation might be the protection affected by *Trep. cuniculi* infection. In the authors' laboratories " at times both yaws and *cuniculi* spirochaetes produce lesions which exhibit in the experimental animal many of the characteristics of syphilitic lesions, but we have never been able to establish that this altered response signified a permanent change in any particular strain of yaws or *cuniculi* spirochaete." There is no evidence, within historical times, that syphilis has derived from yaws or *vice versa*. Perhaps, in fact, one or both of them originated from venereal spirochaetosis of rabbits, or *vice versa*. *T. cuniculi* is believed to be non-pathogenic for man, but further study is needed.

Resistance of syphilis, yaws, and cuniculi rabbits to challenge inoculation of heterologous strains of T. pallidum, T. pertenue, *and* T. cuniculi *6 months after original inoculation. Results 21 days after challenge inoculation*

Original infection intratesticular	Rabbits in group	*T. cuniculi*, strain A			*T. pertenue*, strain YD			*T. pallidum*, Nichols strain		
		Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions		
		No lesions	±,+, ++	+++, ++++	No lesions	±,+, ++	+++, ++++	No lesions	±,+, ++	+++, ++++
None: controls	18	0	16	2	0	14	4	0	0	18
Cuniculi, strain B	18	18	0	0	18	0	0	16	2	0
Yaws, strain YC	18	17	1	0	18	0	0	16	2	0
Syphilis, strain S-6	18	18	0	0	18	0	0	16	2	0

Resistance of syphilis, yaws, and cuniculi rabbits to challenge inoculation of heterologous strains of T. pallidum, T. pertenue, *and* T. cuniculi *6 months after original infection. Results 35 days after challenge inoculation*

Original infection intratesticular	Rabbits in group	*T. cuniculi*, strain A			*T. pertenue*, strain YD			*T. pallidum*, Nichols strain		
		Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions			Rabbits showing indicated size of lesions		
		No lesions	±,+, ++	+++, ++++	No lesions	±,+, ++	+++, ++++	No lesions	±,+, ++	+++, ++++
None: controls	18	1	2	15	3	13	2	0	0	18
Cuniculi, strain B	18	18	0	0	15	3	0	8	6	4
Yaws, strain YC	17*	5	11	1	16	1	0	14	3	0
Syphilis, strain S-6	18	14	4	0	18	0	0	17	0	1

*One animal of the original group died between the twenty-first and thirty-fifth day.

C. J. Hackett

LEPROSY

MOISER, B. **Hansen's Disease (Leprosy) and Cockroaches.** *East African Med. J.* 1947, June, v. 24, No. 6, 230–36, 2 diagrams.

This paper deals with zoological facts regarding cockroaches. The author admits that he had never seen these insects bite man, and failed to get them to do so in daylight, but he accepts statements of others to the effect that they bite at night. They are especially numerous in damp hot climates. In African huts, spraying with 5 per cent. DDT in kerosene kills them in a dosage of a gallon per 100 sq. feet, but the eggs are protected by a chitinous envelope; the cycle from the ova through four or more nymphal stages to adults occupies a year. A detailed description is given of the anatomy of cockroaches and it is stated that the wounds made by the chitinous mouth parts as a result of biting are characteristic, being circular or oval and varying from the size of a pin's head to 4 or 5 mm. in diameter. A method of dissecting the insects is given and the appearances of acid-fast bacilli in their gut are described as in previous papers by the same author [this *Bulletin*, 1947, v. 44, 725]. The occurrence of *Spirochaeta recurrentis* and *Rickettsia* in these insects is referred to, as well as helminths and certain pathogenic bacteria. *L. Rogers*

ZANETTI, V. Coloration en série du bacille de Hansen et dépistage des lépreux bacillaires. [**Staining of Leprosy Bacilli and Diagnosis of Leprosy.**] *Ann. Soc. Belge de Méd. Trop.* 1947, Mar. 31, v. 27, No. 1, 179–86.

This paper deals with the following modification of the carbol-fuchsin method of staining lepra bacilli: First fix by heat and stain for 20 minutes with a cold solution consisting of 1 gm. fuchsin, 10 cc. 95 per cent. alcohol, 5 cc. crystallized phenol, made up to 100 cc. with distilled water. Wash quickly and decolourize for 7 minutes in 0·5 per cent. solution of sulphuric acid. Counterstain for one minute with a solution consisting of 0·15 gm. toluidine blue, 10 cc. 95 per cent. alcohol, 3 gm. crystallized phenol, made up to 100 cc. with distilled water. Wash and dry. The bacilli are stained red with a background of violet. The acid-fast bacilli are estimated in fifty fields in five specimens taken respectively from the ear, the forehead, the cheek, a leprous plaque and from healthy skin.

The results of 2,620 such examinations are discussed. In 252 of these, clumps of bacilli were found in variable numbers in lepromatous cases. The negative cases were clinically of the nerve type, a few reacting cases of which were positive. Repeated examinations show that when very few bacilli are present, they tend to disappear under treatment in four to six months, but in a few cases they increase in numbers with passage of the case into the lepromatous type. In the 252 positive cases showing clumps of bacilli, they were only found in the ears in 73, or 28·97 per cent.; in both the ears and other parts in 134, or 53·17 per cent.; and in the remaining 45, or 17·86 per cent., in other places only. The ear is the site of election for bacteriological examinations. This method gave better results than are obtained by hot solutions of carbol fuchsin and as good as those obtained by Hallberg's method [this *Bulletin*, 1947, v. 44, 591]. *L. Rogers*

SAYAGO, G. Resultados de pruebas tuberculinicas en hijos de leprosos del preventorio "Amparo Santa Cruz" de Porto Alegre (Brasil). [**Tuberculin Tests in the Children of Leprosy Patients in the Amparo Santa Cruz (Brazil).**] *Hospital.* Rio de Janeiro. 1947, Aug., v. 32, No. 2, 163–4.

The English summary appended to the paper is as follows:—

"1. The tuberculin index of 121 children born from leper parents present values comparable to those of other human groups at the same ages (58·4 per

100 reactors in lepers' sons and 52·9 per 100 reactors in children of an orphans' asylum).

"2. In 42 lepers' sons non reactors to the tuberculin test, the Mitsuda reaction (lepromin reaction) was positive in 92·8 per 100."

SCHUJMAN, S. El valor del chaulmoogra en el tratamiento de la lepra. I. Diferente evolución de los casos de lepra tuberculoide en los adultos tratados y no tratados con la medicación chaulmoógrica. [**The Value of Chaulmoogra in the Treatment of Leprosy. Course of Tuberculoid Leprosy in Adults.**] *Prensa Méd. Argentina.* 1947, July 4, v. 34, No. 27, 1215–25, 9 figs. [17 refs.] English summary.

Some practitioners speak of chaulmoogra with enthusiasm as to its success in the treatment of leprosy, others equally detractingly of it. This divergence is explained, says the author, by their referring to different forms of the disease, the former to the benign tuberculoid type, the latter to the malignant lepromatous type.

The present article is concerned with the tuberculoid form. In infants so affected, but left untreated, there is an early and spontaneous reaction against it and retrogression takes place. This is not so with adults. The author bases his conclusions on more than 400 cases seen during a period of 17 years. If untreated, the primary lesion extends and secondary lesions appear, or, more rarely, the condition remains stationary; it does not clear up. If the primary lesion is excised, but no other treatment adopted, recurrence *in situ* follows. If chaulmoogra is given in small doses, *i.e.* inadequately, gradual retrogression is observed, as one would expect; similarly, if treatment is abandoned when initial improvement occurs. *H. Harold Scott*

HELMINTHIASIS

KHAW, O. K. **An Investigation on Schistosomiasis.** *Chinese Med. J.* Shanghai. 1947, May–June, v. 65, Nos. 5/6, 129–32.

"An investigation on the possibility of schistosomiasis being introduced into India by West African troops who were infected with *S. haematobium mansoni* [presumably *S. mansoni*] and *S. haematobium* revealed:—

"a. That there were no known snail hosts of the parasites in India.

"b. That there was no infection of the local snails, nor could they be experimentally infected under field conditions.

"c. That there were no cases of the disease among the indigenous population amongst whom the West Africans had lived in intimate contact, and using in common the same sources of fresh water, stocked with gastropod molluscs."

[See this *Bulletin*, 1947, v. 44, 599; but also 1945, v. 42, 742.]

BOSCARDI, F. Studi sullo sviluppo e sulla struttura di *Schistosoma haematobium* nel mollusco ospite intermedio. [**The Development and Structure of *Schistosoma haematobium* in its Molluscan Host.**] *Riv. di Parassit.* Rome. 1947, June–Sept., v. 8, Nos. 2/3, 67–83, 10 figs. English summary.

This article will interest helminthologists who wish for information on the life-history of *Sch. haematobium* and in the pathological changes which its presence and growth cause in *Bulinus* and *Physopsis*. The article is crammed with detail and to grasp these the original must be referred to, but the findings may be summarized. Serial sections made soon after the miracidium enters

the mollusc show that penetration does not take place by the skin but by the mouth; the primary sporocyst develops and invasion of the tissues takes place and in the daughter-cysts the forked cercariae develop. Only one miracidium develops in a snail, some sort of immunity seems to prevent invasion by a second miracidium. Photomicrographs are clearly reproduced illustrating the development of the parasite and the tissue changes set up in the snail host.

H. Harold Scott

BOIRON, H. & KOERBER, R. Contribution à l'étude de la bilharziose urinaire en Afrique occidentale française. [**Urinary Schistosomiasis in French West Africa.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 118–24. [13 refs.]

The authors briefly review some of the work done since 1905 in French West Africa, on urinary schistosomiasis. After quoting a series of figures, they conclude that the most active foci of this disease are round Dakar, Kaolak and Fatick in Senegal, the forest region of French Guinea, the Saharan and Soudan regions of Niger, the coastal area of Dahomey, the Ivory Coast, and the basin of the Volta in the French Soudan. They mention particularly 5 foci, after noting that the disease is found along the chief water routes, whereas the coastal areas (except Dakar) are less affected. These foci are:—(1) Along the Niger and its tributaries (Milo, Baoulé and Bagoé) from its source to Timbuktu. (2) The old focus in Haute-Volta, associated with the Volta and its tributaries. (3) The river Senegal and its tributaries. (4) The rivers Gambia, Casamance and Saloum. (5) Dakar. They also mention foci in contiguous areas of the British territories of the Gambia and the Gold Coast.

The authors themselves examined 580 schoolboys at Medina and 3,160 soldiers of the garrison of Dakar. In the former, 14·8 per cent. showed haematuria, and in 6 per cent. eggs of *Schistosoma haematobium* were found. Eggs were also found at a single examination in 13 per cent. of the soldiers indigenous to French West Africa—lower rates were found in a few from the Cameroons and in 422 who originated from Madagascar. The authors, however, think that 15 and 20 per cent. respectively would probably more correctly represent the incidence in the schoolboys and the local troops, arguing that a single examination cannot reveal all cases.

The authors discuss briefly some aspects of the pathology of schistosomiasis, concluding that in West Africa this disease cannot be regarded as a factor in the incidence of primary cancer of the liver. They have used intramuscular pentamidine in treatment of a few cases, with apparent success, but they have not been able to keep under observation for more than a short time the 15 patients so treated.

Charles Wilcocks

VOGEL, H. **Hermaphrodites of** *Schistosoma mansoni*. *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 266–77, 6 figs.

The author describes bisexual males of *S. mansoni*, recovered from infected laboratory animals. These worms, in addition to showing the ordinary characters of males, were provided with an ovary which, when well-developed, contained typical egg-cells; in some, a well-defined oviduct and a uterus were present, although a female genital pore could never be clearly seen. The author notes that these hermaphrodites tend to occur in less suitable hosts, such as guineapigs and rabbits, but not in the recognized "good hosts" such as man and monkey, and only rarely in mice; on the other hand, they occurred frequently in hamsters, which are regarded as suitable hosts in every respect. The scarcity of female worms in guineapigs containing hermaphrodites suggested that the absence of the female partner might be another factor in causing the development of female organs in the male.

In order to test this theory, a number of guineapigs, hamsters, and mice, were exposed to male cercariae only, control animals simultaneously infected with both sexes of cercariae being kept for comparison. The results of these experiments were as follows :—Two guineapigs infected with both sexes yielded 70 male worms, of which three (4·3 per cent.) were provided with a female germ-gland, whereas two guineapigs infected with male cercariae only, yielded 83 males, of which 36 (43·4 per cent.) contained an ovary. Hamsters infected in the same manner yielded similar results ; thus, four hamsters exposed to cercariae of both sexes were subsequently found to harbour 51 male *S. mansoni* of which only one was an hermaphrodite ; while, in contrast to these findings, two hamsters exposed to male cercariae only, were found to harbour 92 male worms, of which 37 (40·2 per cent.) possessed an ovary. Mice used as hosts gave quite different results, for, out of 56 male worms recovered from bisexually infected mice, 1·9 per cent. showed an ovary, whilst amongst 247 males from mice exposed exclusively to male cercariae, a smaller proportion, 1·2 per cent. were hermaphrodites.

Vogel, having shown that the appearance of female characters in the male worm is associated with development in an unsuitable host in the case of guineapigs, and is stimulated by the absence of the female partner in the case of guineapigs and hamsters, then discusses the causal explanation for the phenomenon. GIOVANNOLA [this *Bulletin*, 1936, v. 33, 955] records the finding in a rabbit, previously exposed to male cercariae only, of three pairs of *S. mansoni in copula*, each pair consisting of two males. The author of the present paper records similar findings at autopsies on animals infected by him with male cercariae and notes that in such instances, the large worms, which play the part of the male partner, contain only male genital organs, whereas the small embraced males are hermaphrodites. In view of these findings, he suggests the possibility that residence in the gynaecophoric canal, which is essential to sexual maturation of the female, may likewise stimulate the development of rudimentary female characters in the male. *R. M. Gordon*

MORENAS, L. Fistules à distance et indurations fessières. Séquelles de bilharziose intestinale. [**Fistulae and Induration of the Buttocks after Intestinal Schistosomiasis.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 3/4, 86–8.

The author describes a patient who suffered for many years from a series of fistulae [sinuses might be a more accurate word] which developed on the buttocks and on the posterior surfaces of the thighs. The cause of these was obscure, but in 1936, some years after the sinuses had first begun to appear, eggs of *Schistosoma mansoni* were found in the faeces. Eggs were never found in discharges from the fistulae though these were often examined. The mucous membrane of the rectum appeared to be normal on rectoscopy.

The Wassermann reaction was negative ; a Frei test was not possible, but the patient was seen by Favre himself, and a diagnosis of lymphogranuloma inguinale was rejected. The author considers the conditions to be a sequel of schistosomiasis, although a course of treatment with anthiomaline failed to influence the disease. *Charles Wilcocks*

HALAWANI, A. **Intensive Treatment of Schistosomiasis with Trivalent Antimony Compounds.** *J. Egyptian Pub. Health Ass.* 1946, Nov., v. 21, No. 9, 219–26.

Halawani's paper begins with a list of seven antimonials used in the treatment of schistosomiasis, but proves to be a reiteration of two previous papers dealing with the " intensive " use of Repodral, said to be identical with Fouadin.

These papers were noticed in this *Bulletin*, 1947, v. 44, 220 and 329, and the present article does not appear to contain anything new. *William Alves*

DA SILVA, L. C. T. Tratamento da esquistosomíase de Manson pelo stiboplex. [**Treatment of Schistosomiasis mansoni by Stiboplex.**] *Rev. Brasileira Med.* Rio de Janeiro. 1947, July, v. 4, No. 7, 513–17, 3 figs.

The drug used, Stiboplex III, is a golden-yellow powder containing 8·1 per cent. metallic antimony and 33·5 per cent. iodine ; it is soluble in a mixture of equal parts of [unspecified solutions of] sodium tartrate and urethane, and in 1 per cent. propylene glycol at 24°C. The same strength in water at this temperature is not quite all dissolved.

The author gives details of experimental work with this compound on artificially infected guineapigs, and on its action on the worms *in vitro*. Three mgm. of the drug in 1 per cent. watery solution daily for 3 days killed the worms in the guineapigs ; for the *in vitro* tests solutions were prepared varying between 0·7 and 0·0015 per cent. of tartar emetic, Repodral and Stiboplex III. Even the highest dilution of tartar emetic immobilized the worms ; this result was obtained by the 0·0054 per cent. dilution of Repodral and the 0·0109 per cent. of Stiboplex, but tartar emetic contains 0·35 gm. metallic antimony per gramme, whereas Repodral contains 0·136 and Stiboplex III 0·081 gm. per gramme.

Four human cases in which it was tried are detailed ; all had undergone splenectomy. It will suffice to record more fully one of the four, for they are all very similar. A lad of 16 years had for some time been feeling weak and incapable of effort, and complained of digestive disturbances, diarrhoea with liquid stools containing mucus, more recently a rise of temperature, palpitation, dyspnoea ; the liver was enlarged, edge two fingers' breadths below the costal margin, and the spleen was enlarged to the level of the umbilicus ; no malaria parasites were found ; red corpuscles 3,375,000, leucocytes 4,000 per cmm., eosinophiles 6 per cent. ; in the faeces were ova of *S. mansoni*, *Ascaris lumbricoides*, *Necator americanus*, *Trichuris trichiura* and *Strongyloides stercoralis*. Splenectomy was performed without mishap ; 7 weeks later, he was given an intravenous injection of 2 cc. Stiboplex solution ; three days later 3 cc., the next two doses of 5 cc. at 3-day intervals ; after 6 days, he was given 7 cc. at 3-, 3- and 4-day intervals, all intravenously. He also had daily injections of 20 cc. of 50 per cent. glucose and vitamins C and B complex. After the second 7 cc. dose, examination of the faeces revealed no ova of *Sch. mansoni* [nothing is said of the other infestations] and the blood showed an eosinophilia of 42 per cent. [total leucocytes not stated] ; in another patient, subsequent to the treatment, the eosinophiles made up 61 per cent.

The author acknowledges that four cases are too few for any generalization, but says that treatment should be " based on the principle of increasing doses at short intervals of 1 to 3 days, at a rate of 10 to 12 endovenous injections, starting with 3 cc. of the commercial solution to 7 to 8 cc. for adults."

H. Harold Scott

JANSEN, G. Profilaxia experimental da esquistosomose de Manson. [**Attempts at Prophylaxis of Schistosomiasis mansoni.**] *Mem. Inst. Oswaldo Cruz.* 1946, Sept., v. 44, No. 3, 549–78, 20 figs., 1 chart & 1 map.

This paper is a sequel to, or amplification of, the author's publication of 1943 [this *Bulletin*, 1945, v. 42, 1018]. He presents a line map of the Catende district and several photographs depicting the terrain, the construction of model baths, wash-houses and latrines. He examined, once each only, the faeces of 6,559 persons and found ova of *S. mansoni* in 3,482 (53·1 per cent.). The faeces were diluted with water, passed through fine gauze, centrifuged and

the deposit examined microscopically. The results are given in age-groups. Of 651 up to 40 years of age 6·6 per cent. were positive ; of 730 between 5 and 9 years 37·1 ; of 780 between 10 and 14 years 66·0 ; of 1,607 between 15 and 24 years 71·7 ; of 1,158 in the next decade 61·1 ; after which a steady decline was observed to 35·4 per cent. of 288 over 55 years. The vector is *Australorbis centimetralis*.

Of the drugs used for treating human cases the most successful was tartar emetic ; 1,348 were thus treated and 1,159, or 85 per cent. were cured. Maciel's method was adopted, 1 per cent. solution injected *intra venam*, 0·05 gm. on the first day, and, if there was no appreciable reaction, 0·1 gm. the next day, till 0·95 gm. has been given in 10 injections. If there are signs of intolerance, such as diarrhoea, nausea, vomiting and cough, the dose is reduced again to 0·05 gm. The next best drug was stibetin intravenously, 97 being cured out of 160 (56·8 per cent.) ; the same drug intramuscularly cured only 42 out of 292 (14·3) ; antimonyl, on the other hand, proved better by the intramuscular than by the intravenous route, but the number treated intramuscularly was very small, only 12, of whom 5 were cured ; of 117 injected intravenously 39 (31·1) were cured ; stibin intramuscularly cured 11 out of 50 (22 per cent.).

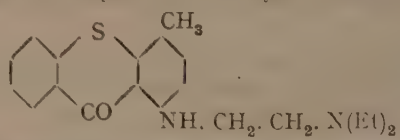
H. Harold Scott

PAK, C. **Studies on Acquired Tolerance to Tartar Emetic, Antimony Sodium Thioglycollate and Neostam.** *Chinese Med. J.* Shanghai. 1946, July–Aug., v. 64, Nos. 7/8, 181–201, 4 figs. [12 refs.]

An investigation of the various factors which may produce tolerance to antimony was studied in rats and mice ; tartar emetic, antimony sodium thioglycollate and neostam were used. The decrease in lethal effect of the drug following the administration of one or more initial doses in different percentages of the lethal dose, and after various time intervals between the doses, was used as a criterion of tolerance. In rats, about 50 per cent. of the lethal dose given initially was optimal for producing tolerance and in the case of tartar emetic a single initial dose was satisfactory. In other cases, the best method of spacing the doses differed for rats and mice. If the interval between initial doses of the drug was too short, a sensitivity to the substance sometimes developed. The mechanism of development of tolerance is discussed. Both tri- and pentavalent antimony compounds were found not to be cumulative in action and each type is equally effective in producing tolerance. The toxicity of tartar emetic was notably increased by starvation of the experimental animals. *J. D. Fulton*

LATNER, A. L., COXON, R. V. & KING, E. J. **Measurement of the Concentration of Miracil in Biological Fluids.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Sept., v. 41, No. 1, 133–40, 3 figs.

Miracil (1-diethylaminoethylamino-4-methyl-thioxanthone)



was synthesized in Germany and gave promising results in the treatment of experimental schistosomiasis. Methods for its estimation in biological fluids are described in this paper. The fluorimetric method proved unsatisfactory. That of BRODIE & UDENFRIEND (*J. Biol. Chem.* 1945, v. 158, 705) applied by KING *et al.* [this *Bulletin*, 1946, v. 43, 822] to the estimation of paludrine by laking with a dye was tried by the present authors, but has not been fully developed.

They finally adapted a simple colorimetric method, in which the yellow colour produced by miracil extracted from 5 ml. of blood and dissolved in 0·04 N HCl was read in a Spekker absorptiometer with ultra-violet light and special filter. By this means, 10 to 100 μg/100 ml. could be estimated. After the blood was haemolysed by distilled water, the mixture was made alkaline and then extracted twice with ether, which was in turn washed with alkali and water, and then extracted with HCl of definite concentration before readings were made in the absorptiometer. The amount of miracil present was determined from a calibration curve. Recoveries of miracil added to blood varied from 80 to 110 per cent. Similar results were used for estimating miracil in urine and the error was not greater than 10 per cent. *J. D. Fulton*

PESIGAN, T. P., TORRES, L. F., Jr. & RECIO, P. M. **Paragonimiasis Westermani : an Unexpected Case with Cystic Formation in the Anterior Abdominal Wall.** *J. Philippine Med. Ass.* 1947, July, v. 23, No. 7, 293–8, 2 figs. on 1 pl.

WU, K. *Fasciolopsis* **in Guinea Pigs with a Summary of the Definitive Hosts.** *Chinese Med. J.* Shanghai. 1946, July–Aug., v. 64, Nos. 7/8, 219–23, 4 figs. on 1 pl.

Experimental feeding of *F. buski* cysts to 16 guineapigs gave one positive result, in which immature worms were found in a guineapig which died prematurely. From this and previous investigations it is concluded that these animals are probably not suitable for laboratory work with *F. buski*. Previous work, by the author and other authorities, on the definitive hosts of this worm is summarized in a table. *J. J. C. Buckley*

VON BONSDORFF, B. **Does Feeding of** *Diphyllobothrium latum* **influence the Interaction between the Intrinsic and the Extrinsic Factors of Castle ?** *Diphyllobothrium latum* **and Pernicious Anemia VIII.** *Acta Med. Scandinavica.* 1947, Oct. 15, v. 129, No. 1, 59–76, 8 figs.

" The addition of fresh or dried Diphyllobothrium latum has not the power to nullify the antianemic effect of mixtures of extrinsic and intrinsic factors when given to patients with cryptogenetic pernicious anemia, the administration of dried worm does not hinder the remission after worm cure in pernicious tapeworm anemia, and the admixture of dried worm to hog's stomach preparations does not diminish their therapeutic effect."

ALLEN, R. W. **The Thermal Death Point of Cysticerci of** *Taenia saginata.* *J. Parasitology.* 1947, Aug., v. 33, No. 4, 331–8. [11 refs.]

" 1. A series of experiments was carried out to determine the thermal death point of cysticerci of *Taenia saginata*. After the cysticerci were exposed to various temperatures, attained gradually, they were tested for viability by the use of one or all of the following criteria : (1) ability to evaginate in warm sodium taurocholate solution, (2) activity of flame cells, and (3) the ability to pass through the digestive tract of man without being digested.

" 2. Decapsulated cysticerci heated to temperatures as high as 54°C. evaginated partially in sodium taurocholate solution and showed active flame cells in some cases. A small percentage of those heated to 55°C. evaginated partially in taurocholate solution but none showed active flame cells. Those heated to 56°C. did not respond in taurocholate solution, did not show active flame cells, and were completely digested when passed through the digestive tract of a human subject.

"3. Cysticerci that were heated in muscle tissue to temperatures as high as 50°C. evaginated in taurocholate solution and showed active flame cells. A small percentage of those heated to 55°C. evaginated partially but none showed active flame cells. However, 3 out of 6 were not completely digested when passed through the digestive tract of a human subject. Cysticerci heated gradually in muscle tissue to temperatures of 56°C., and those that were heated to 57°C., did not respond in taurocholate solution, did not show active flame cells, and were digested when passed through the digestive tract of a human subject."

SURRACO, N. L. & GALEANO MUÑOZ, J. Primer caso documentado, en el Uruguay de parasitismo humano por *Hymenolepis diminuta*. [**First Recorded Case in Uruguay of Human Infection with** *Hymenolepis diminuta*.] *Arch. Uruguayos de Med., Cirug. y Especialidades*. 1947, Apr., v. 30, No. 4, 370–78, 5 figs. [10 refs.] English summary (5 lines).

A case in a child aged 4.

LARSH, J. E., Jr. **The Rôle of Reduced Food Intake in Alcoholic Debilitation of Mice infected with** *Hymenolepis*. *J. Parasitology*. 1947, Aug., v. 33, No. 4, 339–44.

A suggestion that malnutrition, brought about by alcoholic debilitation, may have been an important factor in weakening the resistance of young mice to infection with *H. nana* var. *fraterna*, as previously demonstrated by the author [this *Bulletin*, 1946, v. 43, 759], led to the present studies. Having demonstrated that alcoholic mice consumed much less food per day than non-alcoholic controls, the latter were forced to fast daily during the experiment so that their food intake was about the same as that of the alcoholic mice, and after infection they showed a percentage development of cysticercoids which was about the same as that of the alcoholic mice but considerably higher than that of the non-alcoholic, non-fasting controls. Thus the effect of the alcohol in reducing resistance to *Hymenolepis* infection is indirect and operates by interfering with the normal food intake. Subsequent tests showed that this reduced resistance was mainly due to avitaminosis. *J. J. C. Buckley*

LASNIER, E. P., ARDAO, H. A. & CASSINELLI, J. F. Estudio del tejido de granulación de la adventicia de un antiguo quiste hidatico del higado operado. [**Structure of the Granulation Tissue in the Adventitia of an Old Operated Hydatid Cyst of the Liver.**] *Arch. Uruguayos de Med., Cirug. y Especialidades*. 1947, Apr., v. 30, No. 4, 399–414, 6 figs.

YANNICELI, R., SUAREZ, H. & CASTRO CASAL, E. Granuloma hidatidico pulmonar en el adolescente. [**Hydatid Granuloma of the Lung in an Adolescent.**] *Arch. Uruguayos de Med., Cirug. y Especialidades*. 1947, Apr., v. 30, No. 4, 391–8, 5 figs.

VALDES RUIZ, M. & SALAR LUIS, E. Quiste hidatidico del bazo. [**Hydatid Cyst of the Spleen.**] *Med. Colonial*. Madrid. 1947, Oct. 1, v. 10, No. 4, 207–20, 1 fig.

CELENER, D. & ORLANDI, M. A. R. Hidatidosis abdóminopelviana. [**Abdomino-Pelvic Hydatid.**] *Prensa Méd. Argentina*. 1947, July 11, v. 34, No. 28, 1288–92, 2 figs. [37 refs.]

Report of a case.

BENAIM PINTO, H. Aspectos cardio-vasculares de la anquilostomiasis, con especial referencia al problema de la miocarditis crónica. [**Cardiovascular Disturbances in Ankylostomiasis, with special reference to the Question of Chronic Myocarditis.**] *XII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora. No. 26*. Caracas. 1947. 452 pp., numerous illustrations. [Bibliography.]

This exhaustive work was presented as a thesis for the M.D. degree of the Central University of Venezuela. The question of chronic myocarditis is a serious one in Venezuela ; its causes are several and the problem is not purely medical but also economic and social. Circulatory disturbances arise in part from dietetic causes, in part from syphilis, in part from trypanosomiasis (Chagas's disease), in part from schistosomiasis, and in part from ankylostomiasis. The last is dealt with fully in this thesis ; the first also comes into play in association with hookworm disease ; the other known causes receive mere casual mention.

It is estimated that there are some two million persons in Venezuela harbouring hookworms, more than half the total population, and the concomitant circulatory disturbances are of general clinical importance and of interest to many others than specialists and cardiologists. Some of the associated symptoms have been ascribed hitherto to " hookworm anaemia ", but much of the cardiac distress, perhaps to a degree resulting in death, is due to myocarditis.

This volume takes up and discusses minutely various aspects of the problem, mostly with quotations or abstracts from other authors. There are more than 500 references in the bibliography. The author's observed cases numbered 28 ; their ages ranged between 8 and 70 years ; only six were children ; 17 were males, 11 females ; all the men were agricultural workers, the women did domestic work, occasionally helping in the fields. The degree of anaemia was severe : red cells 960,000 to 2,960,000 per cmm., with an average of 1,759,350 ; haemoglobin 10–50 per cent., average 29 ; six were suffering from schistosomiasis and others had syphilis also ; only 14 could be considered as suffering from uncomplicated hookworm myocarditis. The commonest symptoms were dyspnoea, praecordial oppression, vertigo, tinnitus and headache ; oedema, pulsating jugulars, hydropericardium in one patient, hydrothorax in two [recorded as 3·5 and 7 per cent. respectively], anasarca in six, gallop rhythm in eight. The chief pathological change in the heart was a fatty degeneration referable to the anaemia, with cellular infiltration, interfibrillar oedema and increase of connective tissue—all non-specific. Secondary hepatic lesions were naturally present. Each of the 28 cases has a detailed report, with, in most instances, reproductions of the electrocardiograms which are very clear, and X-ray photographs of the thorax, less clear. *H. Harold Scott*

LIE KIAN JOE. *Trichostrongylus* **Infection in Man and Domestic Animals in Java.** *J. Parasitology*. 1947, Aug., v. 33, No. 4, 359–62.

Post-mortem examinations of 119 Indonesians and 32 Chinese revealed *Trichostrongylus* infections in 49 and 6 respectively. *T. colubriformis* was present in every positive case while *T. axei* was found 11 times, in Indonesians only. The number of worms in one individual is usually very small, but in one instance over 5,000 were collected. The duodenum and upper part of the jejunum are the most common habitats.

Experimental infections of a human volunteer were carried out, with larvae of *T. colubriformis* cultured in faeces of a naturally infected goat. These were successful by the oral method, but cutaneous exposure gave negative results.

Similar experiments with *T. axei* were negative. Young goats were easily infected with *T. colubriformis* larvae from human sources ; both in this and in the human experimental infection, 21 days elapsed between exposure and first appearance of eggs in the stools.

No symptoms of sickness accompanied the human infections, but there was a transient eosinophilia to 10 per cent. *J. J. C. Buckley*

FAIN, A. Répartition et étude anatomo-clinique des filarioses humaines dans le territoire de Banningville (Congo Belge). (*Wuchereria bancrofti*—Cobbold, *Filaria loa*—Guyot, *Dipetalonema perstans*—Manson, *Dipetalonemv streptocerca*—Macfie et Corson, *Onchocerca volvulus*—Leuckart). [**Survey and Anatomical and Clinical Study of Human Filariasis in Banningville (Belgian Congo).**] *Ann. Soc. Belge de Méd. Trop.* 1947, Mar. 31, v. 27, No. 1, 25–63, 7 figs. [22 refs.]

The observations upon which this paper are based were made in the Banningville Territory (Belgian Congo) which is situated between 16 and 19° long. E. intersected by 4° lat. S.

The territory is watered by important rivers of which the principal are the Kwango to the east and Kasai to the west. The population is sparse, grouped in villages and hamlets of 100–200 persons. Two thousand five hundred Africans were examined, and these comprised about one-tenth of the adult population. Thick blood-films stained by Giemsa were employed.

A focus of *W. bancrofti* of the periodic type producing clinical manifestations described in other endemic regions was studied for the first time in the Belgian Congo along the course of the Kwango river. The endemic area is confined to the course of the larger rivers.

Several specimens of the adult stage of this worm were obtained for the first time in the medical history of the Congo. The females were entwined in association with the males, usually enclosed in cavernous tissue ; the males, on the other hand, were often found free and extended, making their way through healthy tissue ; thus, several were discovered in the centre of the testis.

Adenopathies and lymphatic varices, and hydroceles were most frequently encountered, and elephantiasis affects about 4 per cent. with predilection for the lower extremities. Filarial lymphangitis was not encountered.

Several small endemic foci of *Onchocerca volvulus* were discovered in Banningville territory. The only clinical signs observed were cysts or nodules almost exclusively confined to the iliac cysts.

There appears to be no relation between the presence of subcutaneous cysts and the presence of *O. volvulus* microfilariae in the skin. About twice as many people harboured microfilariae in the skin as did those who exhibited cysts. On the other hand, cysts containing viable microfilariae may be present and at the same time the latter may be absent from the skin.

Of greater interest is the discovery of *Dipetalonema streptocerca*. This classification is adopted on the authority of PEEL and CHARDOME [this *Bulletin*, 1947, v. 44, 339], who have shown that the parasite of the chimpanzee is almost identical with that of man. The distribution of this filaria is regulated by little-known factors. On the whole, it predominates in the south, but it is also found along the course of the Wamba and Kwango rivers. No clinical manifestations were observed in association with this parasite. It may possibly be coincidental that it is closely associated with goitre.

Acanthocheilonema perstans is uniformly distributed amongst the native population. The average percentage may be as high as 60. The riverside villages are more heavily infested than those more remote from the larger rivers.

No clinical manifestations were observed.

Loa loa is rare in the territory, and the few cases encountered were probably imported. This is probably explained by the absence of the insect vector.

P. Manson-Bahr

DILLER, W. F. **Notes on Filariasis in Liberia.** *J. Parasitology.* 1947, Aug., v. 33, No. 4, 363–6.

Diurnal and nocturnal blood surveys for filariasis were carried out on Liberian natives. Blood smears taken by day from 2,134 persons gave 14 cases of *Wuchereria bancrofti* and 2 of *Acanthocheilonema*, while those taken at night from 955 showed 8·7 per cent. positive for *W. bancrofti* and one case of *A. perstans*. Many cases of elephantiasis were observed, of which scrotal enlargement was the principal type. A blood survey of 431 American soldiers who had been stationed in Liberia for a year or more proved negative for microfilariae.

Dissections of 649 mosquitoes, mostly *Anopheles gambiae*, gave evidence that this species is the probable vector of *W. bancrofti* in the area.

J. J. C. Buckley

CULBERTSON, J. T., in collaboration with H. M. ROSE, HERNANDEZ-MORALES, F., OLIVER-GONZALEZ, J., FIGUEROA ORTIZ, L., RUIZ REYES, F. & NETTEL, R. **Experimental Chemotherapy of Filariasis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, Sept., v. 41, No. 1, 18–43, 1 pl. & 1 chart. [11 refs.] **Discussion** 44–54, 1 chart [WENYON, C. M. (President); ROGERS, L.; NAPIER, L. E.; HAWKING, F.; FAIRLEY, N. H.; MANSON-BAHR, P.; GOODWIN, L. G.; JOHNSTONE, R. D. C.; CULBERTSON, J. T. (in reply)].

CULBERTSON gave an account of the experimental work done by himself and his colleagues on the chemotherapy of *Litomosoides carinii* infections in cotton rats (*Sigmodon hispidus*); of *Wuchereria bancrofti* infections in man; of *Loa loa* infections in man; and of *Onchocerca volvulus* infections in man.

In cotton rats, naturally infected with *Litomosoides carinii*, it was observed that intensive treatment with pentavalent antimony cures the infection [see this *Bulletin*, 1944, v. 41, 772 and 1947, v. 44, 229]. The adult worms live in the pleural space of the rat, and microfilariae occur in the blood. Antimony compounds, such as neostam, neostibosan, and solustibosan, kill the adult parasites in 2 weeks or less, as shown by autopsy, a single massive dose of the drugs often being effective in this; microfilariae, however, linger in the blood, possibly after a temporary drop in number, for months, but once they vanish they do not reappear. The adult worms are evidently much more vulnerable to treatment than are the microfilariae. On this important observation is based a re-examination of the drug treatment of the human filariases.

One hundred and twenty-nine Porto Ricans, shown to be infected with *W. bancrofti*, but only 3 of whom had clinical evidence of their infections, were variously treated with 4 pentavalent antimony compounds (neostibosan, neostam, urea stibamine and stibanose), with 3 trivalent antimony compounds (fouadin, anthiomaline and tartar emetic), and with an arsenical (melarsen oxide) [see this *Bulletin*, 1946, v. 43, 54, 354, and 763]. Microfilarial counts were made on each patient, at a fixed hour, in 60 cmm. of nocturnal blood; when these failed to yield microfilariae, 10 cc. of blood were examined by a concentration technique. Fifteen control persons were similarly observed. These latter continued to show microfilariae throughout the period of observation; but in those cases treated with the drugs, microfilariae vanished in a considerable number of instances after some months. The results of treatment are summarized in the following table :—

Drug	Number of patients treated	Number of patients freed of microfilariae
Neostibosan	35	25
Neostam	11	5
Urea stibamine	6	4
Stibanose (Solustibosan)...	5	1
Fouadin	15	3
Anthiomaline	20	7
Tartar emetic	4	0
Melarsen oxide	18	8

The drugs were given in high dosage to produce these results and some of them, especially fouadin, produced severe drug reactions ; neostibosan was the most satisfactory and was well tolerated. The blood levels of antimony attained with the various compounds did not bear a constant relationship to the successful eradication of the infection ; and the destruction of the adult worms did not lead to elephantiasis or other physical signs of filariasis in the patients. The author does not consider that any of the drugs tried so far are ideal agents for therapeutic use ; and he recommends caution in treatment, lest this prove more hazardous to the patient than the infection.

Three patients suffering from *L. loa* infections, all of whom had, or had had, Calabar swellings, but only one of whom had microfilariae in the blood, were given an intensive course of neostibosan for two weeks. The two patients with recurring Calabar swellings ceased to suffer from these ; and the one with microfilariae, but no current swellings, 15 months later had only 8 per cent. of the number present before treatment.

Forty Mexican patients with onchocerciasis, nearly all of them with severe ocular manifestations, three being blind, were divided into two equal groups. One of these groups was treated intensively with neostibosan intravenously for two weeks, and the other was kept as a control. Several of these patients, towards or after the end of the course of treatment, became frankly ill as a result of it, and one died 3 days later with evidence of renal damage. None of the controls was ill. The estimation in these patients of the levels of their infection rested on counts of microfilariae in skin snippings taken from each cheek and each side of the neck, irrespective of the site of any nodules which might be present. As a result of the unfortunate fatality it proved difficult to follow the cases adequately ; however, one patient was studied for 5 months, and seven others for 10 months. On comparison with the controls, it is difficult to find any evidence of permanent effect of the treatment on the microfilarial levels of *Onchocerca volvulus* in the skin snippings of these patients.

[This paper should be consulted in the original by those interested. It contains detailed information that it is impossible to summarize ; the dosages of the drugs used, and other relevant data, are set out in numerous tables and charts.]

In the discussion which followed, ROGERS recapitulated his pioneer observations on the treatment of *W. bancrofti* infections with sodium antimony tartrate [see this *Bulletin*, 1920, v. 15, 234 and 1921, v. 17, 85] and he now thought that CULBERTSON'S demonstration of the lengthy survival of microfilariae in the blood after successful treatment confirmed his original belief that he had successfully destroyed the adult worms in his cases. He then discussed the aetiology of the periodical attacks of febrile lymphangitis which are a feature of Bancroftian filariasis. After summarizing the records in the literature on the

drug treatment of this infection, he suggested that ALVES and BLAIR's intensive treatment with trivalent antimony salts [see this *Bulletin*, 1946, v. 43, 344] was worthy of investigation in this connexion.

NAPIER recorded some experiences in the treatment of filariasis over 25 years in Calcutta. He concluded that a number of cases of filariasis suffering from kala-azar must have been cured of their infections by the antimonials employed in the treatment of the latter disease. He thought the failure to demonstrate the curative action of these drugs in his cases of filariasis was due to the fact that examinations were not pursued for sufficiently long to recognize that cure had been achieved.

HAWKING referred to the treatment of filariasis in E. Africa with various compounds, more particularly fouadin which was pushed to the toxic limit, and considered that the failure to appreciate the effect of these compounds was attributable to ignorance as to the longevity of microfilariae, a subject on which light had now been thrown by CULBERTSON and his colleagues. He remarked on the ease with which *Litomosoides* infections can be maintained in cotton rats in Britain through the vector mite, *Liponyssus bacoti*, and referred to the infectability of ordinary laboratory rats, mice, hamsters and Orkney voles; but he considered these unsuitable for chemotherapeutic work as the infections are light, and tend to die out spontaneously. He made some observations on the activity of various compounds on experimental filarial infections, and stated he had found arsenical compounds even more active than antimonials, and that half-grown immature worms are much more resistant to drugs than fully-grown worms, which might account for some of Culbertson's failures to cure.

Hamilton FAIRLEY, MANSON-BAHR, GOODWIN, and JOHNSTONE also contributed to the discussion. In reply, CULBERTSON dealt with some of the many points raised and concluded with extracts from Manson's diary, written in 1892–93, suggesting that Manson had demonstrated some therapeutic action of thymol in a case of filariasis carefully observed at intervals for 12 months. *A. R. D. Adams*

WHARTON, D. R. A. **Pathological Changes in Natural and Experimental Filariasis in the Cotton Rat.** *J. Infect. Dis.* 1947, May–June, v. 80, No. 3, 307–18, 15 figs. [18 refs.]

" Pathological changes in the cotton rat, *Sigmodon hispidus*, infected with the filarial worm, *Litomosoides carinii*, are here described. The only clinical sign associated with the infection is a palpable spleen. The infection gives rise to the formation of papillary nodules that may cover the visceral and parietal pleura. The nodules arise from a proliferative edematous reaction of the pleura followed by infiltration of lymphocytes, neutrophiles and eosinophiles, and, later, plasma cells and fibrocytes. Thick laminated fibrosis and enlargement of the lymphatics of the pleura occur in heavy infections.

" The lung tissue shows scattered eosinophilia and hypertrophy of the lining alveolar cells. Eosinophilia is characteristic of the pulmonary blood but not of the peripheral blood. The larger bronchioles may be involved in a markedly eosinophilic edematous reaction suggestive of asthma.

" Living microfilariae are numerous in the pulmonary vessels but are not centers of reaction. The size of the spleen is two and one-half times that of the normal organ. The spleen shows follicular hyperplasia. *Bartonella* has not been observed. Peritoneal and occasionally inguinal lymph nodes may be enlarged.

" The differential white blood cell count appears essentially unchanged.

" Adult worms may migrate through the mediastinum or be immobilized and destroyed there.

"The pathological effects here recorded have been reproduced experimentally in normal cotton rats. The reaction in the host seems to be due primarily to excretions of the living adult worms and not necessarily to the disintegration of dead worms. Circulating living microfilariae appear to have little if any effect. The reaction is characterized by edema and eosinophilia and is considered to be predominantly allergic.

"The significance of these findings in relation to the pathological changes in human filariasis and elephantiasis is discussed."

DEFICIENCY DISEASES

KODICEK, E., CARPENTER, K. J. & HARRIS, L. J. **"Pellagragenic" Action of Maize. Further Experiments.** *Lancet.* 1947, Oct. 25, 616–17. [12 refs.]

In 1946 the authors reported [this *Bulletin*, 1947, v. 44, 119] that growth-rate in rats is retarded by the addition to their diet of indole-3-acetic acid, a substance of which a precursor is present in significant amounts in maize. This effect was counteracted by the addition to the diet of either nicotinic acid or tryptophane.

In subsequent trials, these results have not been consistently reproduced. A number of control animals on the basal diet have shown depression of growth and the proportion of rats on the indole-3-acetic acid diet showing retardation is no longer significantly greater than in the control series. Other workers have experienced similarly irregular results.

Rats given a 40 per cent. maize diet do, however, show the same retardation, curable by nicotinic acid or tryptophane, as was previously observed.

In the search for a possible toxic factor in maize, the maize-meal was extracted by a procedure designed to remove the indole-3-acetic acid and which, at the same time, removed a protein fraction. Rats fed on the extracted meal showed little or no growth retardation; feeding experiments with the extract and with fractions derived from it have so far given inconclusive results.

It is suggested that the erratic responses observed by several workers in this field may be due to change in the bacterial flora of the intestines and consequent change in microsynthesis, possibly brought about by the prolonged use of synthetic diets.

The present findings make it seem very unlikely that indole-3-acetic acid can be responsible *as such* for the apparently more constant "pellagragenic" activity possessed by maize. *Dean A. Smith*

PÉREZ, J. C. La pelagra en la República de Bolivia. [**Pellagra in Bolivia.**] *Hospital.* Rio de Janeiro. 1945, Oct., v. 28, No. 4, 543–57. English summary.

A general account of pellagra, the origin of its name, the history of the disease, its causation and symptomatology, followed by the narration of a case in a man of 35 years in Cochabamba, who is believed to have contracted the disease owing to the low diet resulting from the war between Bolivia and Paraguay. Cure was obtained rapidly from administration of nicotinic acid in tablets of 0·05 gm. taken twice daily before the principal meals, in combination with injections of liver extract [form and dose not stated] which the author thinks is a valuable adjuvant to the nicotinic acid. *H. Harold Scott*

SPRUE

i. FRAZER, A. C. **Aetiology of Steatorrhoea.** *Brit. Med. J.* 1947, Oct. 25, 641–5, 3 figs. [22 refs.]

ii. BLACK, D. A. K. & FOURMAN, L. P. R. **Some Problems of Tropical Sprue.** *Ibid.* 645–7. [11 refs.]

ii. BRITISH MED. J. 1947, Oct. 25, 660–61. [13 refs.] **Fat Absorption and the Sprue Syndrome.**

i. Steatorrhoea is observed in tropical and non-tropical sprue, coeliac disease, pancreatitis, gastro-colic fistula and other conditions. The process of fat absorption may be divided into an intraluminar phase (when it is prepared for absorption), an intracellular phase (in which the fatty material passes through the intestinal cell), and a distribution phase (when the fat is dispersed from the intestine by various pathways into the body).

Intraluminar phase.—Fat is digested as triglyceride and there is no doubt that the fat is finely dispersed as an emulsion of particles less than $0{\cdot}5\,\mu$ in the lumen of the small intestine.

In normal persons, the contents of the upper two-thirds of the intestine are acid (*p*H 6·5) and fat is absorbed in triple combination-fatty-acid-bile-salt-monoglyceride.

It may be concluded that long-chain triglycerides are partially hydrolysed in the upper part of the small intestine to fatty acids and lower glycerides, and that these two substances, with bile salts, provide the emulsifying system by which the remaining glycerides are dispersed into fine particles.

These changes normally occur in tropical and in non-tropical sprue and in regional ileitis, but not in conditions which interfere with any of the essential components of the emulsifying system.

Intracellular phase of Fat Absorption.—Many water-soluble materials appear to pass through the outer membranes of the intestinal cell. Fatty acids pass into the intestinal cell possibly in the form of soaps.

Severe cases of sprue may show marked disturbance of water and electrolyte metabolism.

It has been suggested that adrenal cortical deficiency may be an aetiological factor in the sprue syndrome, but on the other hand, patients with non-tropical sprue can be relieved of any suggestive signs of adrenal insufficiency by appropriate treatment, without any change in the quantitative aspect of the fat-absorption defect.

Under special experimental circumstances, re-synthesis of triglyceride can be demonstrated *in vivo*. There is little evidence that it is an important feature in normal fat absorption. It seems possible that one important function of phosphorylation in the intestinal cell is to provide phospholipid for the change in interfacial film structure which must occur if the fat particles are to remain in a dispersed state in the protein environment of the bloodstream.

The author discusses the action of choline, and the theory that a defect in phosphorylation may be an aetiological factor in sprue.

Deficiencies of riboflavin or nicotinic acid are frequently associated with fat-absorption defects, especially the sprue syndrome. It is possible to obtain dramatic relief of signs and symptoms of deficiency by administration of the appropriate vitamins, without any measurable change in the fat absorption defect. Ariboflavinosis and other vitamin deficiencies occur, in which fat-absorption is normal. It may be concluded that vitamin deficiencies, except, possibly, that of choline, are probably not concerned with the aetiology of fat-absorption in sprue.

Distributive Phase of Fat Absorption.—Fat may be absorbed by at least two distinct mechanisms, each of which uses a different distributive pathway. The proportion of fat which is absorbed in particulate form may be reduced, with a corresponding increase in fatty acid absorption. The main factors which seem to be concerned in changes in the distributive phase, apart from obstruction in the lymphatic pathway, are the *p*H in the intestinal lumen and the composition of the dietary triglyceride.

ii. Neutral fat is absorbed as a very fine emulsion, and when absorbed, enters the lacteals and alternately the systemic blood stream, when it may be visible as fine particles (chylomicrons). Split fat, on the other hand, enters the portal system and may be absorbed without increasing the chylomicrons. In practical experience, the authors have found the chylomicron count of limited value as a measure of fat absorption in view of the great variation in the size of the particles.

The authors used three methods of studying fat absorption in patients, namely chylomicron counts, serum lipid curves and fat-balance experiments. As the result of experience they came to rely mostly on the last method. A significant difference was established between the fasting values in 9 normal persons and 16 patients with sprue ; in the latter the total fat was only slightly lower than normal ; after the meal, the increment in total fatty acid in those with sprue was only about half that in the normal persons ; but the normal range of fat curve was very wide, so that in the individual patient with sprue the curve might fall within the normal range. It was found that variation between successive four-day stool collections was very great, and in order to reduce error all results have been considered in twelve-day periods.

The excretion of fat can introduce only a small systematic error.

Normal people taking a mixed diet containing 50 to 100 gm. of fat daily will absorb over 90 per cent. of it ; but in 28 patients with early tropical sprue, fat absorption ranged from 50 to 85 per cent.

In therapeutic trials with nicotinic acid and riboflavin in large doses, no improvement in clinical state or fat-absorption was observed. Large doses of crude liver extract produced rapid clinical improvement, but no detectable change in the percentage of fat absorption after several weeks, and thereafter only a slow improvement : 15–20 gm. of yeast extract daily, however, given to patients on liver treatment produced some improvement in fat-absorption in the first 12 days. Folic acid likewise may relieve all symptoms of the disease, but does not increase the percentage of fat absorbed. Apart from glucose, the absorption of non-fatty substances in sprue has been little studied. If unabsorbed carbohydrates were as easily recognizable in the stools as are unabsorbed fats, the demonstration of impaired carbohydrate absorption in sprue might not have to be based on the equivocal evidence of blood-sugar curves which are so easily modified by non-absorptive factors. The evidence on this question is mostly indirect. Some general impairment of absorption was suggested by the finding that in the active stages of sprue the dry weight of the stools was increased to a greater extent than could be accounted for by their increased fat content. Iodide and amino-acids were abnormally absorbed. The evidence suggests that there is a fairly general impaired absorption in sprue and that fat malabsorption has been first observed only because its effects on the stools are more obvious.

Salt deficiency.—In severe sprue, the serum sodium and chloride were both found to be low. It was shown that large amounts of sodium and chloride were lost in the watery stools. Sodium was practically absent from the urine, although chloride was still present in half the normal amount. This represents the biochemical pattern of salt deficiency accompanied by some acidosis.

Two findings are of practical therapeutic significance. Yeast extract in large doses exerts a favourable effect on fat-absorption. Secondly, a number of patients become acutely ill with salt deficiency dehydration associated with watery diarrhoea. In such patients, the diarrhoea must be controlled with sulphaguanidine and parenteral liver and the diet supplemented with moderate amounts of salt.

iii. The editorial discusses the significance of these two papers and refers to other relevant work : it concludes that, " if our understanding of the physiology of fat absorption is imperfect, enough has been said to show that the absorptive defects in the sprue syndrome are even more mysterious." *P. Manson-Bahr*

GELFAND, M. **Sprue and Coeliac Disease in Tropical Africa.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1947, v. 41, No. 1, 109–18.

The author has seen, and reports a case of, coeliac disease presenting the classical picture in an African child of 5 ; and he also reports a case of this condition in a European child of 2½ years. Both cases were rather milder in type than those encountered in Europe, and both did well under treatment.

It is generally held that tropical sprue is rare, if it occurs at all, in the dark-skinned races. The author has not seen this disease in an adult African. It is also said that sprue is rare in Europeans in Africa. Since 1941, the author has seen three elderly Europeans with incomplete sprue, in Rhodesia. All were originally diagnosed as suffering from malignant disease, in view of the wasting ; all recovered on suitable dietary treatment.

Kwashiorkor (infantile pellagra) occurs in young children (1½ to 4 years) throughout most of tropical and subtropical Africa. The author considers the condition *not* primarily dietetic in origin for the following reasons :—The onset is abrupt, in an apparently healthy child ; the mother and other children in the family are usually well ; the diets of the affected children appear to be adequate ; and kwashiorkor would not be so fatal if it were of nutritional origin, especially when it is diagnosed early and treated with an adequate diet. Suspecting that kwashiorkor might be due to jejunal deficiency, the author performed fat analyses on some cases ; in some there was steatorrhoea, in others none ; the results therefore do not support this thesis, or that kwashiorkor is a sprue-like disease. The author's belief is that it is primarily a liver disorder and at 3 autopsies he has observed a yellow fatty liver in each case. [Full data are given of examples of each type of case the author discusses.]

A. R. D. Adams

SUAREZ, R. M. El efecto de los conjugados de acido folico en el espru. [**Folic Acid Conjugates in Sprue.**] *Bol. Asoc. Med. de Puerto Rico.* 1947, Aug., v. 39, No. 8, 281–9.

An account of 4 cases.

HAEMATOLOGY

COURDURIER, J. & BRYGOO, E. Considérations sur la vitesse de sédimentation des hématies chez les Noirs en Afrique. [**The Blood Sedimentation Rate in Africans.**] *Méd. Trop.* Marseilles. 1947, May–June, v. 7, No. 3, 254–9. [16 refs.]

In the Hygiene Institute at Douala the authors studied the blood sedimentation rate in 50 healthy ex-service Africans from different parts of the Cameroons. Westergren's technique was used and tests were made each day

at the same time and under identical conditions. Readings were recorded after one and two hours. The average readings were 38·2 and 57·3 respectively, but the variations were so great (0 to 137 for the first hour : 2 to 145 for the second) that these averages are of little value.

The authors discuss the various factors which might account for these high rates. While they were unable to disprove entirely any meteorological or racial influences, they do not consider that these were significant. Many parasitic infestations were found and these are discussed. The authors believe that these must be taken into account in assessing what constitutes a " normal " African—those in apparently good health, " living with their parasites " and living active lives would constitute normal people. The authors believe that the anomalies in the B.S.R., including the wide range of figures which made the establishment of an " average " reading impracticable, can be accounted for entirely by the high degree of parasitism encountered in apparently healthy Africans.

In the circumstances, the B.S.R., which is regarded as having a real value in Europe, cannot be considered of much assistance in French Equatorial Africa.

H. J. O'D. Burke-Gaffney

VAN UFFORD, W. J. Q. Over de Bloedbezinkingssnelheid in de tropen. [**Blood Sedimentation Rate in the Tropics.**] *Med. Maandblad.* Batavia. 1947, July, No. 12, 220–22.

VENOMS AND ANTIVENENES

CHRISTENSEN, P. A. & DE WAAL, Mara. **Magnesium Sulphate and Carbolic Soap as Antidotes in Snake-Bite.** *South African Med. J.* 1947, Sept. 27, v. 21, No. 18, 680–81.

The good reports on the use of injections of magnesium sulphate solutions by SHIRCORE [this *Bulletin*, 1947, v. 44, 1017, and see also 1927, v. 24, 900, and 1943, v. 40, 625] and of 5 per cent. carbolic soap solution by AHUJA and BROOKS [*ibid.*, 1946, v. 43, 478] called for confirmation and both have been tested by the present authors in a properly controlled series of experiments. In the first, Shircore's method was followed closely. Dried venom of *Bitis arietans* was reconstituted in saline and 0·2 cc. (equivalent to 4–5 m.l.d. for guineapigs) was injected into the hind-leg muscles of each of 16 guineapigs and 5–10 minutes later 8 were infiltrated with local injections of 10 per cent. magnesium sulphate solution, the other 8 serving as controls. All 16 were dead within 3½ hours. The magnesium sulphate clearly was valueless against puff-adder venom. Next, the protective value of the $MgSO_4$ solution and of the soap were tested against the venoms of *Naja flava* (the Cape Cobra), *Sepedon haemachates* (the ringhals), and *Bitis arietans* (the Puff-Adder). The m.l.d. (0·06 mgm.) of the cobra venom was injected as before and 5 minutes later 9 guineapigs received 1 cc. of the sulphate solution, 9 the same amount of soap solution, 9 received 0·25 cc. antivenene, and 9 were left as controls. With the *Sepedon* venom the same method was used, but 0·5 ml. of antivenene : the *Bitis* venom was injected subcutaneously into the flank instead of intramuscularly, because of the damage effected by the latter route, and 2 cc. of antivenene were injected. In a third test, the cobra venom was re-tested, with the use of 0·2 mgm. (or about 3 m.l.d.) and 40 animals were injected, 10 for each method of treatment, and 10 untreated controls. The results are

presented in a detailed table, but they may be stated briefly thus : the $MgSO_4$ proved valueless ; the carbolic soap solution was definitely protective against the cobra and the ringhals, useless against the puff-adder venom ; it is to be recommended, therefore, as a first-aid treatment for cobra bites.

H. Harold Scott

DE MAGALHÃES, O. O combate ao escorpionismo. [**Against Scorpions.**] *Mem. Inst. Oswaldo Cruz.* 1946, Sept., v. 44, No. 3, 425–39. [21 refs.]

The question of dealing with scorpions is a serious one in parts of Brazil. Scorpion sting may be fatal even to adults, but even when it is not fatal it causes much pain, suffering and distress. In Belo Horizonte, 1,221 cases were recorded in 1941 and in three years 2,529, and, of course, many patients did not consult a medical man and so were not recorded. *Tityus serrulatus* seems to be the commonest and *T. bahiensis* next, but there are also two species of *Parabuthus*, *P. transvaalicus* and *P. triradulatus* ; two of *Opisthophthalmus*, *O. wahlbergi* and *O. glabrifrons*, and *Hadogenes trogloditis dentatus*.

DDT, or Neocid in powder, is effectual in killing the scorpion after an interval ; for treatment of stings, the appropriate serum given early is the best.

H. Harold Scott

MACCHIAVELLO, A. **Cutaneous Arachnoidism or Gangrenous Spot of Chile.** *Puerto Rico J. Pub. Health & Trop. Med.* 1947, June, v. 22, No. 4, 425–66, 5 figs. [Refs. in footnotes.] [Spanish version 467–505.]

The author presents a picture of the *mancha gangrenosa*, or gangrenous spot, of Chile. It results from the injection of a necrotizing poison by a spider, *Loxosceles laeta*. Clinically, arachnoidism in Chile may be divided into three groups : (1) Cutaneous ; (2) viscero-cutaneous ; (3) nervous ; the last due to the Black Widow spider, *Latrodectus mactans*.

Cutaneous arachnoidism is more common in the northern zone of Chile, from Antofagasta to Copiapó and Ovalle ; rare, but not unknown, in the central area ; cases are more often seen in the spring and summer, October–April, and more particularly January–April, but in some years no cases are seen. *Loxosceles laeta* is a house-spider, so most cases are " domestic accidents."

The symptoms of cutaneous arachnoidism, gangrenous spot, are nearly always purely local—sharp pain becoming a burning sensation ; there are local oedema and erythema which spread, then the swelling hardens, darkens to violet or black by the third day ; necrosis of the underlying tissue occurs (sometimes with a covering blister) and sloughing of a large surface up to 30 cm. or even more in 2–3 weeks. There may be keloid development later. Strange as it may seem, apart from the first day's pain and insomnia, which are not relieved by morphia, there are no constitutional symptoms. Details of 25 cases illustrating the above are given.

In the viscero-cutaneous form, the same spider is the cause and the reason for the production of generalized symptoms (such cases are few) is thought to be the injection of the poison directly into some vessel of the skin. In these patients there are rise of temperature, haematuria, jaundice, asthenia and vomiting. Red corpuscles are reduced by some 60 per cent. whereas the leucocytes are increased to about the same degree. Differentially, the chief change is an increase in large monocytes at the expense of the polymorphonuclears.

Study of the poison shows that it is not of itself haemolytic and the pathogenesis of the haematuria awaits explanation. The difference from the bites

of *Latrodectus mactans* rests in the absence of general symptoms and the localized coagulant and necrotic action, whereas *L. mactans* has a special action on the nervous system and the symptoms are generalized. *H. Harold Scott*

DERMATOLOGY AND FUNGUS DISEASES

DORMER, B. A. & SCHER, P. **Case Report X. Tumour of the Lung due to *Cryptococcus histolyticus*.** *Clin. Proc.* Cape Town. 1947, Aug., v. 6, No. 6, 269–73, 6 figs.

NEGRONI, P., FERNÁNDEZ, L. L. & DAGLIO, C. A. N. A proposito de un caso de pie de Madura con granos negros. Revisión de los micetomas producidos por "Madurella". [**Concerning a Case of Madura Foot with Black Grains. Review of the Mycetomas caused by *Madurella*.**] *Rev. Argentina Dermatosifilologia.* 1947, June, v. 31, No. 2, 192–205, 3 figs. [34 refs.] English summary (8 lines).

The authors present a review of the history and nomenclature of the species of the genus *Madurella* Laveran, and supplement this with an analytical table of the reported characters of the fungi. They also describe the fungus from a case of black grain mycetoma from Argentina, which they have identified as *Madurella ramiroi*, da Silva. A fungus from the same lesion had previously been diagnosed as *Aspergillus chevalieri* by two other pathologists.

[The time is ripe for a revision of the species of *Madurella*, some of which are based on a study which did not include the examination of the fungus in saprophytic culture, and there is little doubt that several of the specific names should be treated as synonyms of *Madurella mycetomi*.] *J. T. Duncan*

DE ALMEIDA, F., RIBEIRO, D. O., ASHCAR, H., LACAZ, C. da S. & SAMPAIO, S. de A. P. I. Ação da penicilina, "in vitro", sôbre o paracoccidioides brasiliensis. II. Resultados obtidos com a administração dêsse antibiótico no tratamento da "blastomicose sul-americana". **I. Action of Penicillin on Cultures of *Paracoccidioides brasiliensis*. II. Results of Administration of Penicillin to Patients suffering from South-American Blastomycosis.**] *Hospital.* Rio de Janeiro. 1946, Jan., v. 29, No. 1, 181–4, 1 fig.

I. Reports on the action of penicillin on mycotic fungi have been discordant; the studies of KEENEY, AJELLO and LANKFORD (*Bull. Johns Hopkins Hosp.*, 1944, v. 75, 410) led them to conclude that "The use of penicillin in the treatment of the superficial and the deep mycotic infections is unwarranted and contraindicated." The present authors, nevertheless, resolved to test its effect on cultures of *Paracoccidioides brasiliensis*. In each of four tubes of Sabouraud broth, *p*H 6·4, they placed a fragment of the culture obtained on solid Sabouraud glucose. The tubes were then incubated at temperatures ranging from 24° to 48°C. and when growth appeared, there were added daily to the first three tubes 1, 10 and 50 Oxford units of penicillin respectively, the fourth being left as control. Five days later, examination revealed that in tube 1 there were more than 3·2 units, in tube 2 more than 32, and in tube 3 more than 160 units. In spite of continuing the daily addition of penicillin, at the end of ten days the growth in all the tubes was the same. Photographs of the tubes are reproduced in the article.

II. Penicillin was given to each of three patients suffering from different forms of South American blastomycosis. The first, with the glandular form,

was given 20,000 Oxford units of sodium penicillin intramuscularly every 3 hours. After a total of 600,000 units had been given, treatment had to be suspended because the patient seemed to be "physically worse". The second, with the cutaneous and glandular form, was given 25,000 units every 3 hours intramuscularly, to a total of 1,300,000 units. The third, with the mucous membrane form, was given 50,000 units in the same way to a total of 3,000,000 units. In all three there was observed at first a slight improvement in the cutaneous and mucous lesions, they were softer and less oedematous, but no further amelioration took place. The early improvement is ascribed to the effect of the penicillin on the secondary infections. In short, in the doses given, the penicillin was without action on the blastomycotic condition. *H. Harold Scott*

CAMPOURCY, A. Chromoblastomycose au Cameroun. [**Chromoblastomycosis in the Cameroons.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 7/8, 252–3, 1 fig.

HABIBI, M. *Rhinosporidium seeberi* en Iran. [*Rhinosporidium seeberi* **in Iran.**] *Ann. Parasit. Humaine et Comparée.* 1947, v. 22, Nos. 1/2, 84–8, 4 figs.

Rhinosporidiosis, caused by *Rhinosporidium seeberi*, is a relatively rare mycosis; the total number of reported cases, from all countries, does not exceed 165. Habibi has observed 31 cases in Persia since 1937; before that date the disease had not been recognized in the country.

An analysis of the age incidence in 28 of the Persian cases shows that 10 contracted the infection between the 10th and 20th years, 7 between the 20th and 30th years and 4, 3, 2 and 1 in each of the succceeding decades. Only one patient was under 10 years of age. The disease is not associated with any particular occupation, but the highest number of cases occurred amongst scholars, which may be related to their ages or to the greater possibility of transmission of the infection during play. Geographically, 16 of the cases were connected with Ardebile, 13 with Teheran and 1 each with Ispahan and Kermansha. In 22 cases the polypi arose from the nasal mucosa, in 7 from the conjunctiva of the eye or eyelid and in 2 from both nose and eye. In treatment, strangulation of the polyp at its pedicle with a silk ligature, as practised in the Ardebile district, gives only transient relief followed by recurrence; instillation of a weak solution of tartar emetic, advocated by WRIGHT, proved ineffective, but electro-coagulation of the polyp and its immediate neighbourhood, or surgical excision followed by cauterization of the base of the tumour, gave the most satisfactory results. *J. T. Duncan*

LANGERON, M. *Tritirachium brumpti* (Langeron et Lichaa 1934) Langeron 1947 et le genre *Tritirachium* Limber 1940. [*Tritirachium brumpti* **and the Genus** *Tritirachium.*] *Ann. Parasit. Humaine et Comparée.* 1947, v. 22, Nos. 1/2, 94–9, 1 pl. & 1 fig. [13 refs.]

The fungus described from a case of ocular mycosis in Egypt as *Beauveria brumpti* [this *Bulletin*, 1935, v. 32, 898] is here re-named *Tritirachium brumpti* and four other fungi found associated with disease in man are also transferred to the latter genus. The pathogenicity of these five species of *Tritirachium*, which are, in the author's opinion, normally saprophytes of world-wide distribution, appears to be weak. *G. C. Ainsworth*

HEAT STROKE AND ALLIED CONDITIONS

CONSOLAZIO, W. V., PECORA, L. J. & TUSING, T. **A Slow Dissolving, Non-Irritating Salt Tablet for Use in Hot Environments.** *J. Indust. Hyg. & Toxicol.* 1947, Sept., v. 29, No. 5, 347–50, 2 figs.

Severe symptoms of nausea, vomiting and epigastric discomfort are frequent as a result of the use of ordinary salt tablets to combat the effects of heat and excessive sweating. It was believed at first that these symptoms were due to prolonged contact of the salt with the gastro-intestinal mucosa. Salt tablets prepared with cornstarch to bring about rapid solution were, however, not satisfactory. Slowly dissolving tablets were then prepared on the assumption that with these the salt concentration might never be great enough to cause irritation of the mucosa. These tablets were found to be very satisfactory in a number of trials.

These slowly dissolving tablets are prepared by treating ordinary salt tablets with a solution of cellulose nitrate or acetate and then drying at 100°C. to remove the solvent. This procedure gives rise to the formation of a honeycomb structure. The impregnating film of cellulose weighs about 4 mgm. per tablet of 0·65 gm. In a few experiments no evidence was found of any toxic effects in animals through the ingestion of cellulose nitrate or acetate. The solution time of the impregnated tablet is of the order of eighty minutes, compared with fifteen minutes for the pure salt tablet and one minute for the salt-cornstarch tablet. *M. E. Delafield*

TROPICAL ULCER

LICHTMAN, J. A. **Tropical Ulcer with special reference to its Etiology.** *Clin. Proc.* Cape Town. 1947, July, v. 6, No. 5, 165–86, 14 figs. & 3 charts. [72 refs.]

This paper is based on the personal study of 160 patients treated in Durban, Natal.

It is usually agreed that tropical ulcer may start as :—

(*a*) infection of a wound or other lesion (most commonly) ;

(*b*) spontaneously as a vesicle, which bursts in a few days (probably uncommon.)

Site.—The author in his series found that 41·4 per cent. of ulcers occurred on the anterior surface of the leg in its middle or lower thirds and rarely occurred elsewhere than on the lower extremities [all observers are probably agreed on this]. An adherent yellowish-grey slough at the base of the ulcer was a characteristic feature and pain was a frequent symptom. The chief complication was extension, especially in depth and in 34 per cent. of cases the ulcer had extended to tendon and bone. [Spontaneous fracture of underlying bone has been recorded.]

Surrounding multiple ulcers, indicative of auto-inoculation, were not uncommon, but lymph-spread was not a feature and no cases of malignant change were found in this series (VINT in Kenya found microscopic malignant changes in 2 per cent. of cases examined). Scars of previous ulcers were found in 43 per cent., which does not support the theory that one ulcer confers immunity.

Bacteriology.—Fusiform bacilli were found in 70 per cent., spirochaetes in 60 per cent., but these were always found together with fusiform bacilli. In only 36·6 per cent. were fusiform bacilli and spirochaetes found without other

organisms. Although other organisms such as Gram-positive diplococci, staphylococci and streptococci were met frequently, the predominating ones were fusiform bacilli and spirochaetes.

Diphtheria and diphtheroids were uniformly absent; streptococci were not conspicuous; Leishman-Donovan bodies were not found, either in smears or sections; blastomycosis, actinomycosis, and evidence of other mycotic organisms were not found.

The fusiform bacilli and spirochaetes were morphologically identical with those of Vincent's angina, and the author considers that they are causal and pathogenic for the following reasons:—

1. In 36·6 per cent. they were the only organisms found in active lesions;
2. They are associated with a definite clinical type and can invade living tissue;
3. Tropical ulcer has been reproduced in human beings with pure cultures of fusiform bacilli by intradermal injection plus some form of trauma [see this *Bulletin*, 1946, v. 43, 378].

Trauma undoubtedly plays a large part in causation; and contact with saliva (in which fuso-spirochaetes are often present) is a likely mode of infection.

Climate.—Cases are very rare outside the latitudes 35°N. and 10°S., although the author's series come from Durban, 30°S. Local predisposing causes are probably increased liability to injury due to scanty clothing in hot climates and increased skin moisture predisposing to bacterial growth [*cf.* prickly heat]. The author was unable to incriminate syphilis, malaria, hookworm, bilharzia or anaemia as important predisposing causes, although he does consider that in West Africa sickle cell anaemia may play a part.

Dietary deficiency is undoubtedly a predisposing factor. Thus meat- and fish-eating tribes are much more rarely affected than those whose diet is mainly vegetarian and where the protein is of low biological value [*cf.* the rarity of this condition amongst the Masai, who live mainly on meat, milk, and blood, despite the fact that they live under very dirty conditions and are very prone to injuries of the lower extremities]. The author was unable to find evidence of deficient protein content in the serum of ten consecutive unselected cases; but he does consider vitamin deficiency, especially lack of nicotinic acid and riboflavin, to be an important predisposing cause; he notes the prevalence of "crazy pavement" skin and pigmentation of the legs.

Local predisposing causes.—Dirt and exposure to injury are regarded as important, but the presence of peripheral neuritis was not noted. The paper contains several tables and some excellent photographs.

C. F. Shelton

MISCELLANEOUS DISEASES

CHODZKO, W. **Persistent Endemic Foci of certain Acute Infectious Conditions. Remarks on their Extinction.** *Bull. Office Internat. d'Hyg. Publique.* 1946, Oct.–Nov.–Dec., v. 38, Nos. 10–11–12, 913–34. [40 refs.] [French version 889–912, 3 maps.]

The Polish delegate's report to the Permanent Committee ranges over many diseases and presents again many facts and ideas of interest. It is worth remembering that Ferran was early in the field, possibly the first in the field, with vaccination against cholera in Spain and his vaccine was, like the fixed antirabic virus of Pasteur, a vaccine of living organisms. Mention is made by Chodzko of Rogers' denial that cholera spreads throughout India from Bengal. [One wonders whether an endemic home for cholera, usually allotted to India

and China, might not be found in the valley of the Russian Don ?] Influenza is given its original endemic centre in China, especially in the basin of the Yellow River of North China. An interesting point is made of a freqeunt association, which manifested itself in Poland after the first world war :— epidemic relapsing fever nearly always follows epidemic typhus fever. The phenomenon, which is probably not accidental, although the former is a spirochaetosis and the latter a rickettsiosis, " also occurred in Algeria, Egypt and Roumania following the first and second world wars . . . . Whenever there is a big world-wide conflagration, the hideous face of louse-borne typhus fever appears on the scene ". References are made to the tick-borne and mite-borne typhus fevers and to the great danger of aeroplane introduction of the disease ; to the prophylactic vaccines that are now available, of which the first in order of discovery was the Polish vaccine of Weigl ; to DDT insecticide and to the Soviet antiseptic soap. Plague, although said to have its original endemic centre in central Asia has, at various times, swept over Europe. Sylvatic epizootic plague has, perhaps, received more attention of recent years than epidemic plague. The possibility that plague-infected fleas may travel even by ship, hidden in bales of jute, to start the disease in a distant country is mentioned ; this subject has received recent attention. Smallpox, like those diseases already mentioned, receives a special heading and special commentary. In Russia, vaccination against smallpox " started to be carried out in 1803, but it was not until 1909 that vaccinations and revaccinations were made compulsory by a special law, which was followed by striking success ". Poland freed itself from smallpox in 1919 and " since 1936 not a single case of smallpox has been notified ".

There is again a special commentary on giardiasis as presenting a special pandemic problem. The author reminds us that the causal agent of the disease, originally known as *Lamblia*, owes its name to Professor Lambl, a Czech scientist, and professor of medicine at Warsaw University. The professor himself called the parasite *Cercomonas*. As there are large numbers of carriers of the organism " it would appear necessary to introduce compulsory notification of cases of giardiasis ", which is a " real invisible pandemic disease ".

W. F. Harvey

ASH, J. E. **The Lymph Node in Tropical Diseases.** *Amer. J. Trop. Med.* 1947, July, v. 27, No. 4, 483–91, 10 figs.

In lymphopathia venereum (climatic or tropical bubo) the stellate abscess cannot be differentiated from the granuloma of several other infections, particularly tularaemia. It is closely simulated in filarial infection, but is readily distinguishable from that of tuberculosis and syphilis by the type of necrosis.

In scrub typhus, there is generalized adenitis and the glands may show areas of gross necrosis. In Oroya fever, the lymph nodes are specifically concerned, because of the involvement of the reticulo-endothelial system. A less specific feature is " sinus catarrh ". The sinuses are dilated, the endothelium swollen and the lumina filled with lymphocytes and large macrophages.

In yaws, the treponemata are demonstrable, in the lymph nodes.

The reaction of the lymphatic tissue to *Brucella* bears a considerable similarity to that of Hodgkin's disease. Most pathologists have recognized in brucellosis a non-specific and non-neoplastic reaction—such as is seen after irradiation, and which was observed especially in the tissues of Japanese atomic-bomb victims. In *Brucella* infections, especially of *Br. melitensis* origin, it is seen more particularly in the mesenteric glands and spleen, and includes the presence of multinucleated cells indistinguishable from the Reed-Sternberg cell of Hodgkin's disease.

Typhoid fever is a lymphadenotropic infection with a reaction that is usually characteristic enough to warrant identification in absence of other criteria. The typhoid cell is a large mononuclear cell which tends to collect in foci and displace the normal lymphatic tissue.

In all cases of plague, there is localization of *Pasteurella* in the lymph nodes. The primary localization of the organism is there. The toxin of *P. pestis* causes necrosis of the vessel walls, and the reaction is characterized by extensive necrosis and haemorrhage.

In leprosy, involvement of the lymph nodes is a constant feature, so that diagnosis may be made bacteriologically by aspiration of the inguinal glands. In the early stages, pigmented foam cells are scattered near the cortex and contain bacilli. Histoplasmosis is the only fungous disease with a predilection for the reticulo-endothelial system.

In leishmaniasis the lymph node is not particularly involved, except in heavy infections. The glandular lesions of filariasis (*W. bancrofti*) infections are too well known to need further description. *W. malayi* may localize about the mammary gland or in the axilla. An interesting feature of the histology is that eosinophilia may be present in lymph nodes in which these worms may not necessarily be identified. *P. Manson-Bahr*

SCHWETZ, J. Sur la rivière Fwa (Congo belge). Notes géographiques, zoologiques et médicales. [**Geographical, Zoological and Medical Notes on the River Fwa, Belgian Congo.**] *Inst. Roy. Colonial Belge—Bull. des Séances.* 1947, v. 18, No. 1, 271–95, 1 text fig., 5 figs. on 2 pls. & 1 folding map.

" Lake Fwa " in the Belgian Congo is 155 km. from Lusambo and 135 km. from Luluabourg. Its natural beauty attracted many tourists and a small hotel was built on its banks. Soon after, a large proportion of visitors were infected with schistosomiasis ; a large number of lakeside native dwellers were likewise found to be infected. The hotel was closed ; European visitors ceased to visit the lake ; fishing was prohibited, and the villages were removed to a distance from the banks. The author of this report spent twelve days at Fwa and gives the results of his observations.

" Lake Fwa " is not a lake, but a river of an unusual kind. Gushing springs emit such large quantities of water that the resulting river is very many metres wide near its source. The river flows 15 km. to join the river Lubi ; its width varies from 50 to 200 metres or more.

The author writes enthusiastically of the natural beauties, the fish and birds. Mosquitoes were very abundant. Of 722 specimens identified, there were 601 *A. funestus* ; 99 *A. marshalli* var. *moucheti* and 22 *A. gambiae*. Larvae of three other anophelines were found, *A. coustani*, *A. paludis* and *A. obscurus*. *Phlebotomus* and *Culicoides* were very abundant, *P. africanus*, *P. schwetzi*, *P. decipiens* and *Culicoides inornatipennis*. *Glossina palpalis* was found, but was not abundant along the river banks.

The molluscan fauna was rich : 11 species were found, 10 Gasteropods and 1 Lamellibranch. There were two species of *Planorbis*, *Biomphalaria adowensis* and *Afroplanorbis salinarum*.

An examination of 70 villagers in one nearby village revealed 21 with schistosomiasis, 45 with ankylostomiasis and 28 with ascariasis.

Norman White

DE ALBUQUERQUE, A. F. R. & MACHADO, A. C. Contribuição ao conhecimento da nosologia de Alagoas. [**Disease in Alagoas.**] *Rev. Hig. e Saúde Pública.* 1947, Apr.–June, v. 5, No. 1, 21–34, 2 maps.

Alagoas occupies an area of 28,571 kilometres between 8°55′ and 10°28′ south latitude and 5°15′ and 8°10′ east longitude of the meridian of Rio de Janeiro.

After a brief account of its physiogeography the authors consider three diseases and their vectors, *viz.*, the Triatomidae, yaws and schistosomiasis.

Of 2,338 Triatomidae examined, 2,326 (99·5 per cent.) were *Panstrongylus megistus* and 410 (17·6 per cent.) were infected with *T. cruzi* ; 7 were *Eutriatoma maculata*, one infected ; and 5 were *T. brasiliensis*, 2 infected. A table gives the distribution of *P. megistus* in 23 localities ; most, in actual numbers and in percentage, were in the wooded districts.

Yaws was systematically taken in hand in 1943, treatment units being established. In 17 of the 33 municipalities the numbers recorded for the three years 1943–45 were, respectively, 1,863, 3,523 and 4.625 ; the numbers in the different municipalities are shown in a table [but this would be of local interest only].

Schistosomiasis mansoni is common in the wooded and maritime regions ; the snail hosts are *Australorbis centimetralis* and *A. olivaceus*. Another mollusc, of the genus *Ampullaria*, abounds in the State ; one of these was found parasitized by a forked cercaria in 1943. Ten localities are detailed in a table. In Maceió, of 15,096 persons examined, 893 (5·6 per cent.) were positive ; among 2,646 children in schools in the same district 59 (2·2) were positive ; among 2,341 in the Rio Largo district 738 (31·5) were infested. In other places the percentages positive were high, but the numbers examined were small.

H. Harold Scott

GALLO, P. & VOGELSANG, E. G. Las zoonosis en Venezuela. [**Diseases of Animals in Venezuela.**] *XII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora. No. 27.* Caracas. 1946, 53 pp. [Bibliography.]

An interesting article, not confined to veterinary diseases, as the title would imply, but a consideration of the diseases common to animals and man, or communicable from animals to man. All the usual diseases are mentioned—rabies, encephalo-myelitis, anthrax, parasitic infestations, etc. One section of particular interest is that dealing with animals which act as reservoirs of human disease in Venezuela, as howler monkeys and yellow fever, rats and plague, canine and human leishmaniasis, opossums and armadillos and Chagas's disease, dogs and *Desmodus* and human rabies.

H. Harold Scott

DEMANGE, Jean-Marie. Un myriapode chilopode, *Orphnaeus brasilianus nigropictus* Att. de l'oreille humaine en Équateur. [**A Myriapod,** *Orphaneus brasilianus nigropictus* **Att. from the Human Ear in Ecuador.**] *Ann. Parasit. Humaine et Comparée.* 1947, v. 22, Nos. 1/2, 65–7, 6 figs.

PROTOZOOLOGY : GENERAL

WENRICH, D. H. **The Species of** *Trichomonas* **in Man.** *J. Parasitology.* 1947, June, v. 33, No. 3, 177–88, 3 figs. [Numerous refs.]

The author returns to the subject of the species of *Trichomonas* in man which he previously discussed [this *Bulletin*, 1944, v. 41, 697]. He gives further details for their differentiation and discusses the relevant literature. He concludes that the oral form (*T. tenax*) and the vaginal form (*T. vaginalis*) with four anterior flagella are closely related, while the intestinal form (*T. hominis*) possesses five anterior flagella, four of which arise from a single blepharoplast as do the four flagella of *T. tenax* and *T. vaginalis*, while the fifth originates in a single small ventral blepharoplast. The author is careful to note that *T. hominis* is the only intestinal form he has seen, but admits that forms with three and four flagella may occur. The paper is illustrated by three diagrams showing the structure of the three species discussed.

C. M. Wenyon

KIRBY, H. **Flagellate and Host Relationships of Trichomonad Flagellates.** *J. Parasitology.* 1947, June, v. 33, No. 3, 214–28. [40 refs.]

The author discusses the flagellates of the genus *Trichomonas* and other flagellates that have basic features of structure and a type of cell division comparable to that of *Trichomonas*. Many of the forms considered are parasites of termites. *C. M. Wenyon*

CROSS, Joy B. **A Cytologic Study of *Toxoplasma* with special reference to its Effects on the Host's Cell.** *J. Infect. Dis.* 1947, May–June, v. 80, No. 3, 278–96, 52 figs. on 4 pls. [Numerous refs.]

The author has studied the morphology of toxoplasma as exhibited by two strains maintained in mice. Material from the peritoneum was used and fixation was always by the wet method—Bouin's solution, Flemming's fluid, Schaudinn's fluid, and 10 per cent. formalin. For staining, various methods were adopted, including Feulgen reaction. It is pointed out that in the peritoneal cavity the parasites are both extra- and intra-cellular and when in the latter situation, in spite of their multiplication, they do not interfere with the nuclear division of the host cell. The parasite contains a shadowy band of cytoplasm which divides it longitudinally. This is termed the "cytostyle". Another structure which is occasionally seen is a phlange which stretches from one end of the parasite to the other. It is assumed that the appearance of the parasite as a crescent in dried films is due to the failure of this phlange to stain. Apart from the nucleus, a number of granules are present in the cytoplasm. The nucleus is described as dividing by mitosis with persistence of the nuclear membrane. This is specially clear in specimens stained by Feulgen's method. Reproduction is by binary fission, there being no evidence of any schizogenic process. Eventually the intra-cellular parasites are so numerous that the host cell nucleus is extruded, leaving a terminal colony of parasites surrounded by a membrane representing the remains of the host cell. From her observations, the author concludes that the parasite is a protozoon. In three slides, some 50 flagellated organisms were encountered but the author is uncertain as to their identity. The paper is illustrated by a number of drawings.

[It is perhaps unfortunate that no mention is made of the living organisms as these might have served as controls of the fixed specimens, many of which appear to the reviewer to be abnormalities. In fixed specimens, the prevailing type of nucleus is that of a vesicle with small central karyosome.]

C. M. Wenyon

ENTOMOLOGY AND INSECTICIDES: GENERAL

HILL, Marjorie A. **The Life-Cycle and Habits of *Culicoides impunctatus* Goetghebuer and *Culicoides obsoletus* Meigen, together with some Observations on the Life-Cycle of *Culicoides odibilis* Austen, *Culicoides pallidicornis* Kieffer, *Culicoides cubitalis* Edwards and *Culicoides chiopterus* Meigen.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 55–115, 12 text figs., 5 figs. on 2 pls., 6 graphs. & 2 histograms. [75 refs.]

The primary object of these investigations was to fill in the gaps in our knowledge of the life-cycle of *Culicoides impunctatus* and *C. obsoletus*, the most wide-spread and annoying "midges" in Britain.

The paper contains detailed records of twelve months' work in the neighbourhood of Liverpool during 1945–46. It includes a very full survey of the literature on the genus, dealing with the life-cycle, the morphology, British species and laboratory technique.

After describing the site of the investigations, the type of soil, the flora in different plots of ground and the methods and materials employed, the author discusses the experiments made and the conclusions drawn from them. An illustrated account is given of the morphology of all stages of the different species. Data from the experiments are presented in full.

For the collection of adults, netting, light-traps and human baits were first employed but were later abandoned. Daily collections were made in the summer of 1945 before sunset each evening as the insects alighted on a black cloth suspended above the ground. Adults were bred in the laboratory in lamp chimneys and feeding was first done on the sorter's arm but later on the shaved ear of a rabbit. Rearing was done in earthenware pots covered with lamp chimneys having organdie fastened over their narrow ends. The medium for *C. impunctatus* was peaty soil and for *C. obsoletus* decaying leaves and mud. Some were kept at 22° to 24°C. but the majority were reared at laboratory temperatures of 16° to 19°C.

From the results of the field and laboratory experiments it was concluded that *C. impunctatus* has a marked preference for human blood. This species was the commonest in the locality and there seems to be one generation per year with a peak in June. Adults began to appear in April and the last were caught in August. They were most active from half an hour before sunset through the night to early morning and did not travel far from their breeding places. Fourth stage larvae were found from November to July, and pupae from April to July. Laboratory studies indicated that the eggs take two weeks to hatch, the larval stage lasts about five months (though some larvae may take as many as seven) and the pupal stage takes 5 days.

C. obsoletus appeared to feed more readily on rabbit's blood than did *C. impunctatus*. There seem to be two generations in a year with peaks in June and September. Eggs hatched within 3 days of laying, the larval stages lasted 3½ to 5 months and the pupal stage 5 days. The life cycle of a strain of this species reared in the field occupied five months in the summer and nine months during the winter.

The more limited observations on the other species indicate that they have but one generation in a year.

H. S. Leeson

HILL, Marjorie A. & ROBERTS, Enid W. **An Investigation into the Effects of "Gammexane" on the Larvae, Pupae and Adults of** *Culicoides impunctatus* **Goetghebuer and on the Adults of** *Culicoides obsoletus* **Meigen.** *Ann. Trop. Med. & Parasit.* 1947, May, v. 41, No. 1, 143–63, 6 graphs. [10 refs.]

The experiments recorded in this paper were made in Knowsley Park, Liverpool, in the summer of 1946. For the experiments on the immature stages, three sites were chosen in damp soil rich with humus, half shaded by rhododendron bushes. Sampling showed that each site contained a similar proportion of larvae and pupae and that they were present only in shaded portions, also that pupation commenced in May. The three plots were sprayed once, in May; one with 5 per cent. Gammexane in miscible oil plus lake water at 100 mgm. Gammexane per square foot; one with lake water only; and the other with miscible oil plus lake water.

Field tests showed no larvae or pupae in the "Gammexane plot" after thirteen days. In the control plots, the number of immature stages increased after the twentieth day until the seventy-seventh day (though there were no pupae after the forty-third day); after the seventy-seventh day the number of larvae decreased until the 126th day, the last of the experiment. No pupae from the "Gammexane plot" produced adults, but those from the controls produced 100 per cent. adults.

Laboratory tests of residual toxicity of soil samples from the "Gammexane plot" showed a continuous increase in the time required to give a 100 per cent. kill of larvae. In the first fortnight, twenty-four-hours' immersion was sufficient, but after the seventeenth week, seven days' contact with the sample of treated soil was necessary to kill all larvae.

Soil penetration tests showed that Gammexane was present in a toxic concentration at a depth of one centimetre during dry weather, but effective penetration was increased to three centimetres after heavy rain and toxicity was still maintained even when the ground was water-logged; however, toxic effects were never observed to extend to a greater depth than three centimetres.

Observations suggest that Gammexane on the soil surface has but a limited effect on ovipositing females, and it is uncertain whether Gammexane exerts any ovicidal action or whether it kills young larvae as they hatch from the eggs. From the experiments with early stages, it is concluded that spraying the breeding places with 5 per cent. Gammexane at 100 mgm. per square foot in May not only destroys the generation of *Culicoides* about to emerge, but also prevents development of adults in the following summer.

In the tests against adults of *Culicoides*, five black cloths, each $1\frac{1}{2} \times 2$ feet, were saturated with 75, 150, 300, 600 and 1,500 mgm. of Gammexane in benzene to give deposits of 12·5, 25, 50, 100 and 250 mgm. per square foot respectively; one other cloth was soaked in benzene only. The cloths were suspended 4 to 5 feet from the ground and left exposed for a month. Alighting midges were collected the first evening, starting one hour before sunset, and ten minutes were allowed for each cloth. Other evening collections were made on four occasions at intervals of six days.

It is shown that the cloth with the highest concentration of insecticide was effective in killing all alighting midges for one week; other treated cloths were less efficient. Toxicity was lost at a steady rate on all cloths, until by the third week it was negligible. It is therefore concluded that this method is not likely to prove satisfactory in the control of adult *Culicoides* except for about two weeks in a restricted area. *H. S. Leeson*

DE MEILLON, B. & GEAR, J. **A Note on Three Noxious Arthropods occurring on the Witwatersrand.** *South African Med. J.* 1947, June 14, v. 21, No. 11, 407–11, 3 figs.

The "Black Widow Spider" *Latrodectus* is found in many areas in Rhodesia and South Africa. Two species, *L. geometricus* and *L. indistinctus* are found. This paper gives some account of the appearance and habits of these spiders, and case records of two severe instances of spider bite are described. Fatalities have occurred and the case mortality rate is approximately five per cent.

This paper also contains an account of the "Tumbu Fly" *Cordylobia anthropophaga*, descriptions of which will be found elsewhere, and also of the plant sucking bug *Pirates lugubris* which sometimes gives a painful bite, although it does not feed on mammals. *Kenneth Mellanby*

OLDROYD, H. **Notes on the Type-Specimens of African Tabanidae (Diptera) described by Mr. H. F. Carter (1912, 1915).** *Ann. Trop. Med. & Parasit.* 1947, Sept., v. 41, No. 2, 234–8, 1 fig.

WOKE, P. A. **Arthropods of Sanitary Importance in the Republic of Nicaragua, Central America.** *Amer. J. Trop. Med.* 1947, May, v. 27, No. 3, 357–75, 1 map.

A list of arthropods collected during brief visits to Nicaragua. It is very incomplete, but as the fauna of this country is imperfectly known, it may be of some value. *Kenneth Mellanby*

JENKINS, D. W. **A Laboratory Method of rearing Chiggers affecting Man (Acarina : Trombiculidae).** Reprinted from *Ann. Entom. Soc. America.* 1947, Mar., v. 40, No. 1, 56–68, 4 pls. [10 refs.]

The author describes his successful experiments in rearing the North American species of *Trombicula*. He reviews earlier work, from which it appears that even the most successful experimenters could only maintain these mites for one generation, and with a high mortality.

Three species are known to occur in the United States: *Eutrombicula alfreddugesi*, *masoni* and *batatas* (? *hominis*): of these the last is confined to the southern States and also occurs in Tropical America. The author generally started his breeding by putting down black cards and collecting unengorged larvae which walked on to them: or he collected wild reptiles which were generally infested and allowed engorged larvae to drop off them. He found that under laboratory conditions larvae of the three species very readily attached themselves to snakes, lizards or turtles (*Terrapene*). The last-named are found to be the most convenient to handle. He also recovered wild larvae by staking out a turtle in a suitable place for a few hours.

In rearing the stages which occur in soil it is necessary to work at high humidity, but to avoid condensation in which larvae may be drowned. It was found convenient to use a jam jar with the bottom removed and a plug of plaster of paris put in in its place. The jar was closed by a screw top through which the larvae did not escape: a hole was drilled in it and plugged with wool. The actual rearing medium was either sterilized humus or loose sandy soil.

In these containers, nymphs and adults fed on eggs of *Aëdes*: if the shell of the egg is moistened, the mite can pierce it and remove the contents in a few minutes. This is clearly an unnatural food, but the extreme neatness with which the mite carries out this task might suggest that eggs of some other insect are a normal food. The mites ate such large numbers of eggs that it was found very difficult to provide enough for the purpose. It seems that the female mites lay an average of about ten eggs per day, a much higher figure than had been expected. The reproductive potential must be high, for the author obtained about 6,000 larvae during two months from a culture containing twenty-three females. The minimum time under which the life-cycle was completed was 50 to 70 days.

The paper contains a large amount of valuable detail. It is clear that the author has maintained these mites for several generations and produced very large numbers of larvae for experimental work. His methods have greatly reduced the amount of handling required and it seems that the mortality was low.

P. A. Buxton

GOODEN, E. L. **Evaluation of Pyrophyllite as an Insecticide Diluent.** *J. Econom. Entom.* 1947, Apr., v. 40, No. 2, 270–73, 3 figs.

Pyrophyllite is a hydrous aluminium silicate, $H_2O.Al_2O_3.4SiO_2$ formed by hydrothermic alteration of volcanic deposits. It is rather difficult to distinguish from talc (the molecules of which are similar, but with 3 atoms of magnesium substituted for two of aluminium) except by the mineralogist's blowpipe test with the use of cobalt nitrate solution.

Pyrophyllite is widely used as a diluent for insecticides in powder form, but there is some controversy about its merits. Three points are important in this connexion :—

(1) Various other minerals are sometimes sold as substitutes (*e.g.* mica).

(2) It is easily confused with talc.

(3) Quartz is sometimes present as an impurity to the extent even of 25 to 30 per cent. This causes an abrasive effect which may have important bearing

on the insecticidal action of a mixed dust. Other dusts used as diluents (*e.g.* talc or kaolin) also may contain quartz and it is important to consider this in making comparisons between these diluents. *J. R. Busvine*

GARNHAM, P. C. C. **Mortality of *Aedes aegypti* feeding on Rabbits receiving Oral " Gammexane ".** [Correspondence.] *Nature.* 1947, Aug. 2, 156–7.

Previous workers have shown that insects may be killed by taking the blood of a mammal fed with DDT (LINDQUIST *et al.*; *J. Econom. Entom.*, 1944, v. 37, 128) or Gammexane [DE MEILLON, this *Bulletin*, 1947, v. 44, 469]. The present investigation used *Aëdes* mosquitoes to determine how long the lethal effect lasted, and the minimum effective doses.

It was found that single doses of 40 mgm. per kgm. of Gammexane given to rabbits killed all *Aëdes aegypti* subsequently feeding on them for about four days. Lower doses were sometimes ineffective shortly after they were given to the rabbits, but later were insecticidal. [This suggests that the concentration of Gammexane in the blood rose, up to twenty-four hours after it was swallowed.] These lower doses were insecticidal for about two days only. It was not feasible to go above doses of 40 mgm. per kgm. which caused convulsions and death in some rabbits. The mosquitoes showed a marked dislike of feeding on treated animals ; few did so and these took smaller blood meals than normal. *J. R. Busvine*

GRANETT, P. & SACKTOR, B. **Testing Tick Repellents and Observations of Phototropic Effects.** *J. Econom. Entom.* 1947, Apr., v. 40, No. 2, 259–63, 9 figs.

In experiments on the efficacy of chemicals as repellents of adults and nymphs of the tick *Amblyomma americanum*, it was observed that the animals were apt to move towards the greater light intensity, *i.e.*, they exhibited positive phototaxis. [The authors' use of the word " phototropism " for this behaviour is to be deplored, as experimental workers restrict the term " tropism " to bending movements such as those exhibited by plants in response to light.] Unless illumination is controlled, phototactic responses may greatly confuse work on repellents. *Kenneth Mellanby*

BRENNAN, J. M. **Preliminary Report on some Organic Materials as Tick Repellents and Toxic Agents.** *Pub. Health Rep.* Wash. 1947, Aug. 8, v. 62, No. 32, 1162–5.

Fifteen chemicals, including several found effective against other pests, were tested for repellency and toxicity to the ticks *Amblyomma americanum* (lone star tick) and *Dermacentor andersoni* (Rocky mountain wood tick). Most of the materials applied to socks, etc., gave 95 to 100 per cent. protection for four weeks following treatment. Rinsing in warm tap water, however, removed most of the protective effect.

None of the compounds immobilized adult ticks confined on treated cloth within two hours, but several stopped nymphs in fifteen to thirty minutes.

The materials included dimethyl and dibutyl phthalates, phenyl cyclohexanol and benzyl benzoate. There were insufficient data to determine the most satisfactory repellent, but a mixture of phenyl cyclohexanol and butylacetanilide seemed most promising. *J. R. Busvine*

HEWLETT, P. S. & PARKIN, E. A. **The Formation of Insecticidal Films on Building Materials. II. Tests of the Efficiency of various Types of Pre-treatment.** *Ann. Applied Biol.* 1947, May, v. 34, No. 2, 224–32, 1 fig.

When the surfaces of building materials (brick, wood, cement, etc.) are sprayed with insecticides to give a residual film, much of the liquid is absorbed into the more porous materials and the availability of the insecticide is lost. In a previous paper (PARKIN and HEWLETT, *Ann. Applied Biol.*, 1946, v. 33, 381) the authors showed that pre-treatment of the building surfaces allowed more effective and persistent films of DDT and pyrethrum to be applied.

In this paper, further substances supplied by manufacturers were tested for pre-treatment effectiveness in improving film formation of pyrethrins in white oil P31. The flour beetle *Tribolium castaneum* was used as the biological indicator.

Thirty substances were subjected to preliminary tests and seven were examined more carefully. It was decided that the necessary qualities of the pre-treatment coating material were that it should be (1) relatively impermeable to the insecticide, and (2) wetted by the insecticide. The two most promising materials were 10 per cent. size and 5 per cent. gelatin ; these will be examined further.

J. R. Busvine

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

SOUTHERN RHODESIA. **Report on the Public Health for the Year 1946** [MORRIS, R. M., Medical Director & Chief Health Officer]. 50 pp. 1947. Salisbury : Rhodesian Printing & Publishing Co., Ltd.

General.—In April Dr. R. R. Morris took over the duties of Medical Director and Chief Health Officer from Dr. Martin who had held the position for 10 years. During 1946, the Commission under the chairmanship of Professor C. M. F. Saint, C.B.E., F.R.C.S., issued their report on the National Health, and another Commission, with Dr. A. J. Orenstein, C.B., C.M.G., C.B.E., as chairman reported on the Colony's leprosy services.

Two new medical stations have been opened, one at Antelope Mine for the Matobo Native District, with a European community and over 80,000 Africans ; the other at Karoi for the settlement there and for the Miami Mica fields and the African reserves of the Zambesi Valley.

Vital Statistics.—The figures for 1941 are inserted in brackets after those for 1946 for purposes of comparison. The European population at the end of June was 83,450 (69,330) ; Asiatics 2,940 (2,570) ; "Coloured persons" 4,590 (3,970) ; native Africans 1,687,000 (1,380,000). European births 2,147 (1,763), birth rate 25·7 (25·4) ; European deaths 687 (696) ; crude death rate 8·2 (10·0) ; infant mortality rate per 1,000 live births 30 (43), the lowest ever recorded in Southern Rhodesia ; maternal deaths 4 (7) ; maternal mortality rate 1·9 (4·0). The chief causes of deaths among Europeans were heart disease and cancer, and of infants premature birth and congenital malformations ; four of the 65 infant deaths were due to malaria.

Diseases.—There were no cases of *smallpox* among Europeans, but 181 among Africans, with only 1 death ; *pulmonary tuberculosis* 36 cases, 3 deaths among Europeans, 323 cases, 89 deaths among the Africans, showing how much greater is the fatality rate among the latter. Of the infective diseases of childhood, *chickenpox* heads the list with 824 cases, 247 Europeans and 577 Africans. *Measles* is next with 345 Europeans and 433 Africans ; *diphtheria*, 282 cases

(51 Europeans, all recovering, 231 Africans with 40 deaths) comes third; *whooping-cough* is fourth, but far behind the others, with 190 cases (84 and 106 respectively) and *typhoid fever* accounted for 108 (24 Europeans, 1 fatal 84 Africans, 9 fatal). There were 30 European and 16 African cases of *acute anterior poliomyelitis*, one death occurring in each group. *Scarlet fever* shows, as elsewhere in the tropics, the greater susceptibility of the European; there was only one African case to 62 European cases, but none was fatal. Admissions of Europeans for *malaria* numbered 1,116, the lowest for 5 years, and for *blackwater fever* 9, the lowest ever recorded in the Colony. It is hinted that this last may be due, at least in part, to the scarcity of quinine and its replacement by mepacrine. *Anopheles gambiae* is the chief vector of malaria. A Research Unit has concentrated on *schistosomiasis*, carrying out treatment of patients and destruction of snails in the same area. Sodium antimony tartrate (SAT) is used, in three injections given slowly on one day only, to a total of 1 grain for each 20 lb. body weight, designed to destroy the female worm and so stop egg-production. Some physicians gave larger total doses of 1 grain per 12 lb. body weight, but this seemed to entail greater risk. No case of *plague*, human or rodent, has been reported. Thirteen cases of *trypanosomiasis*, 5 fatal, have been notified, the highest for 35 years, all from the Zambesi Valley areas. At the beginning of the year there were 1,004 *leprosy* cases registered at the three institutions, Ngomahuru, Myemwa, and Mnene. Five of them were in Europeans. During the year 269 patients were admitted, 140 re-admitted, 84 discharged, 56 died and 51 deserted, leaving 1,222 on the register at the end of the year [not 1,223 as stated].

Hospitals.—There are 14 Government hospitals, European admissions to them totalled 12,236 [elsewhere stated as 11,966], or 146 per mille; in 1941 the respective figures were 11,391 and 164. Maternity beds have been reduced to 118 by the closing of one private maternity home. Native hospital admissions totalled 36,311 and there is much overcrowding, some having to lie on mattresses on the floor or on the verandas. Much medical aid is afforded by *native clinics*, of which there are 73; applications have constantly been made for more to be inaugurated. Inpatients at these numbered 71,620 and outpatients 245,138. Medical Mission clinics, 37 in number, subsidized by the Government, provide 587 beds for Africans; during the year, admissions to these totalled 29,657 and outpatients 166,399.

In the mines, 70,545 were employed, 1,284 fewer than in the preceding year; deaths, 522 (564) were fewer and the rate 7·4 (7·85) per mille was lower. *Venereal diseases* are increasing; both gonorrhoea and syphilis are common in the towns and the mining areas, the main reservoir being native prostitutes.

Laboratories.—There are three routine laboratories, all of which have done excellent work with a small staff assisted by Africans who have proved apt pupils at routine microscopical examinations. Details of the numbers of the different samples and specimens examined are given in lists in Appendices to the report.

Schools.—There are three medical inspectors of schools and school-children and a fourth is to be appointed when a suitable candidate can be found. There is a Government *Dental Service*, with a staff of four qualified dentists whose time has been fully occupied in dealing with over 12,000 children and many other patients.

Health Inspectors do a vast amount of good work. Though there is only an establishment of 16, they inspect premises and supervise general sanitation, food and slaughter-houses; they perform vaccinations against smallpox (347,570 in the year) and against diphtheria (44,230); they have made 23,000 collections of mosquitoes. In some of these activities, they are assisted by Africans.

Nurses are overworked; of a trained staff establishment of 245, only 126 are on the permanent staff; nevertheless this is a great improvement on the previous year when there were only 65. To relieve the pressure, it has been found necessary to engage a number of midwives in the larger maternity homes although they have neither medical nor surgical qualifications. Training of nurses is carried on at Salisbury and Bulawayo hospitals; of 50 candidates at the preliminary examination, 36 passed; of 20 up for the final, all passed, 11 of them with honours. African males are also trained to become nursing orderlies; 31 presented themselves for the lower examination and all but two passed, as did 10 out of 11 at the higher examination. *H. Harold Scott*

CONGO BELGE. Rapport sur l'Hygiène Publique au Congo Belge pendant l'année 1945. [**Report on the Public Health in the Belgian Congo during 1945.**] [LAMBRICHTS, G. P.]. 149 mimeographed pp.

In a preliminary note Dr. Lambrichts points out that it was possible to publish the 1945 and 1946 reports only in 1947; the 1945 report is concerned solely with statistics; commentaries for both years together will be found in the 1946 report.

The 1945 report is a very complete statistical statement and contains a great deal of information, in many cases covering several years. It is on similar lines to the statistical section of the combined report for the war years 1940–1944 [this *Bulletin*, 1947, v. 44, 1024]. *H. J. O'D. Burke-Gaffney*

i. PATERSON, A. R. **The Human Situation in East Africa. Part I. On the Increase of the People. Part II. Towards a Population Policy.** *East African Med. J.* 1947, Feb. & Apr., v. 24, Nos. 2 & 4, 81–90; 144–51.

——. **Summary of some Figures and Opinions bearing on Population Growth.** *Ibid.* 1947, Feb., v. 24, Nos. 2, 90–97.

ii. BRITISH MED. J. 1947, Aug. 9, 214–15. **Planning and World Population.**

iii. MACDONALD, G. **Planning and World Population.** [Correspondence.] *Brit. Med. J.* 1947, Sept. 27, 506-7.

i. These papers by a former Director of Medical Services of Kenya form a detailed consideration of the statements, quoted from the Governor of Kenya, that "it is now evident that taken as a whole East Africa is barely able to support itself in food at the present time," and that "an ignorant man and his wife with a hoe are a totally inadequate foundation for an enlightened state of society . . ."

There is little doubt that the population of Kenya, and of East Africa as a whole, is now increasing at a rate which, if it persists, will present a continuously serious problem in relation to food, agriculture and soil productivity. The rate of increase has been estimated at between 1·5 and 2·3 per cent. per annum. These rates would raise the population of East Africa from just under 12,000,000 in 1935–6 to 34,000,000 or 59,000,000 respectively, in 70 years. Public health measures and freedom from local internecine war will tend to remove certain checks on the growth of population, but the pressure of population, unless it is accompanied by vigorous and enlightened agricultural policy, will result in food shortage and its sequel, disease, which would go far to neutralize public health effort.

Meanwhile, according to the author, the fertility of the soil of Kenya is declining, "by 50 per cent. we are told in the past twenty-five years." [The authority for this is not quoted, and to a reader the bald statements sometimes

made, that the soil of East Africa is naturally poor, are unsatisfactory in the absence of detailed information or proof.] The policy advocated by the author in the face of this most serious threat to the social and economic life of East Africa comprises a complete, synchronized and integrated policy of modernization such as was outlined by NOTESTEIN [this *Bulletin*, 1945, v. 42, 507]. Eventually, the size of families among the Africans will need to be curtailed, but to preach that doctrine to Africans now would be to invite the comment that the object of limitation must be to exterminate them. Control of size of families must therefore be induced by indirect means, by general education and general improvement in conditions of life.

Details of the programme of modernization are quoted from Notestein's paper, but are too full for reproduction here; they include proposals for industrial development and for social advancement.

ii. In the editorial article, similar points are made, and the papers of Paterson are quoted along with others on India and elsewhere. Again are stressed, in relation to East Africa, the three factors: exhaustion of fertility of the soil because of the absence of fallow; ignorance of satisfactory methods of agriculture; and the high rate of increase of the population. The editorial ends as follows: "Yet unless the birth rate falls in relation to the death rate and the population problem is solved much talk about colonial development and welfare is, to use an American expression, 'whistling in the wind'."

iii. Macdonald takes exception to the point of view displayed in the editorial article referred to. He admits that at present rates of increase of population there will come a time when population pressure is too much for the capacity of the land, but he argues that so much of East and South-East Africa is undeveloped, and that so much could be developed with comparative ease if simple methods of tapping ground water were adopted on a sufficient scale, that to speak of reducing population increase is at least premature. He points out that population densities in East Africa vary from 41 to the square mile in Uganda to 5 in Northern Rhodesia, and that enormous tracts of country are uninhabited. "The population problem is one of balance, and the economy of grossly undeveloped countries can be improved more readily and more to the general advantage of the world by an increase in the supportive capacity of the land than by a restriction of population, though ultimately that must come."

Charles Wilcocks

CAROTHERS, J. C. **Age and Wisdom Teeth in Africans.** *East African Med. J.* 1947, Aug., v. 24, No. 8, 304–6, 1 graph.

Medical practitioners in East Africa are frequently faced with the problem of giving an opinion on the age of Africans. This may be a serious responsibility, especially in adolescents, since the law for many purposes regards the East African as being adult if he is apparently 18 years of age or older. Many factors are required in framing an opinion, but there are often great difficulties. If it could be found that wisdom teeth erupted with some constancy at certain ages in Africans, they might prove a useful guide.

The author counted the wisdom teeth of 150 African boys admitted to a High School in Kenya. Many of them claimed to know the date of their births; although the author admits that this unsupported evidence detracts from the value of the enquiry, he has no reason to doubt that they were speaking the truth.

The boys represented a fair sample racially of the population of Kenya. They were mostly between the 15th and 22nd years of life.

The development of the wisdom teeth is shown in a table and depicted in graphic form. From the evidence available, the author observes that "one might draw the following very tentative conclusions:—

"1. The African's wisdom teeth erupt with some constancy between the 15th and 21st birthdays.
"2. If an African has no wisdoms he is unlikely to be more than 20 years old.
"3. If an African has all his wisdoms he is unlikely to be less than 17 years old.
"4. If an African has some of his wisdoms only he is unlikely to be more than 20 or less than 15 years old."

[This form of enquiry merits further investigation on a wide scale, in the search for a solution to a problem so familiar, and often so perplexing, to medical officers in Africa.] *H. J. O'D. Burke-Gaffney*

BOARD OF TRADE. German Industry. B.I.O.S. Final Report No. 1387. **Tropical Medicine at Hamburg and Elberfeld.** [Reported by F. HAWKING.] 26 mimeographed pp., 3 diagrams. 1947. London: H.M. Stationery Office. [2*s*. 6*d*.]

WANNONI, L. L. Contribución al estudio del problema de saneamiento en Venezuela. [**The Health Problem in Venezuela.**] *XII Conferencia Sanitaria Panamericana. Cuadernos Amarillos. Publicaciones de la Comisión Organizadora. No. 28.* Caracas. 1946. 70 pp., numerous charts, figs. & maps.

Venezuela is a country of 912,050 sq. kilometres and a population, in 1941, of 3,849,919. The density of population varies greatly, but is well shown in a sketch map with varying shading. During the quinquennium 1940–44 the chief causes of death were diarrhoea and enteritis [the former is rather a symptom than a disease], tuberculosis, heart disease, pneumonia and malaria. About 5,000 deaths occur annually from "water-borne" diseases—enteric fever, dysentery (amoebic and bacillary) and infantile diarrhoea.

The Ministry of Health and Social Assistance was created in March 1936 and a Division of Malariology the same year and of Sanitary Engineering in 1937. In 1942, a Division to deal with the hookworm question was set up. The need for the last will be clear when we are told that *Necator* infestation ranges between 17 and 91 per cent., with an average for the country of 52 per cent.; that a census of houses revealed that of a total of 668,636 there were 509,306, or 76 per cent., without any arrangement for disposal of excreta. Details of faecal examination of over 13,000 specimens in 46 localities are given in a table; in 8 localities every specimen revealed a positive result and in 29 other localities there were 91–99 per cent. positive. A series of graphs shows the prevalence of this and other helminths in the different districts. *H. Harold Scott*

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ALPHABETICAL LIST OF AUTHORS OR SOURCES

de Albuquerque, A. F. R. & Machado, A. C., 115.
Alkan, W. J., 81.
Allen, R. W., 97.
de Almeida, F., Ribeiro, D. O., Ashcar, H., Lacaz, C. da S. & Sampaio, S. de A. P., 110.
Amaral, A. D. F. & Penido, H. M., 27.
Andrew, R. R., 76.
Angelini, G., 24.
Ash, J. E., 114.
Aubry, G., Laffargue, P. & Portier, A., 19.
Audy, J. R., *et al.*, 62.

Bang, F. B., Hairston, N. G., Maier, J. & Roberts, F. H. S., 45.
de Barros, O. M. & Rosenfeld, G., (55).
Basu, B. C., 26.
Benaim Pinto, H., 99.
Bianco, A. A., Saunders, G. M., Levine, A. S. & Cohn, R., 23.
Bishop, E. L., 46.
Black, D. A. K. & Fourman, L. P. R., 105.
Black, R. H., 25.
Board of Trade, (126).
Boiron, H. & Koerber, R., 93.
Bonne, C., 30.
von Bonsdorff, B., 97.
Boscardi, F., 92.
Boyer, J., 57.
Brackett, S. & Bliznick, A., 80.
Bradley, G. H. & Fritz, R. F., 42.
Brennan, J. M., 121.
British Med. J., 105, 124.
Bull. U.S. Army Med. Dept., 37 *bis*.

Campourcy, A., (111).
Carothers, J. C., 125.
Celener, D. & Orlandi, M. A. R., (98).
Chaudhuri, R. N. & Rai Chaudhuri, M. N., 35.
Chinn, M., 31.
Chodzko, W., 113.
Christensen, P. A. & de Waal, M., 108.
Christophers, S. R., 40.
Congo Belge, 124.
Consolazio, W. V., Pecora, L. J. & Tusing, T., 112.
Cooke, W. E., 76.
Courdurier, J. & Brygoo, E., 107.
Craige, B., Jr., Jones, R., Jr., Whorton, C. M., Pullman, T. N., Alving, A. S. & Eichelberger, L., 33.
Cross, J. B., 117.
Culbertson, J. T., with Rose, H. M., Hernández-Morales, F., Oliver-Gonzalez, J., Figueroa Ortiz, L., Ruiz Reyes, F. & Nettel, R., 101.

Davis, G. E., Austrian, R. C. & Bell, E. J., 70.
De, M. N. & Dutta, P. N., 34.
Delbove, P. & Reynes, V., 61 *ter*.
Demange, J. M., (116).
Dias, A. de C., 58.
Diller, W. F., 101.
Dodd, M. C., 52.
Dormer, B. A. & Scher, P., (110).
Dwinelle, J. H., Sheldon, A. J., Rein, C. R. & Sternberg, T. H., 87.

Eklund, C. M., Parker, R. R. & Lackman, D. B., 71.
Erickson, A. G., 46.

Fain, A., 100.
Fairbairn, H., 50.
Fairley, N. H., 20, 101, (125).
Fleming, R. F. & French, J. M., 75.
Frazer, A. C., 105.

Gallo, P. & Vogelsang, E. G., 116.
Garnham, P. C. C., 121.
——, Davies, C. W., Heisch, R. B. & Timms, G. L., 86.
Gelfand, M., 107.
Giroud, P. & Ciaccio, G., 60.
—— & Jadin, J., 60.
Gooden, E. L., 120.
Goodwin, L. G., 76, 101.
Granett, P. & Sacktor, B., 121.
Greenberg, M. & Pellitteri, O., 71.

Habibi, M., 111.
Hairston, N. G., Bang, F. B. & Maier, J., 22.
Halawani, A., 94.
Hampton, J. W. F., 56.
Hawking, F., 101, (126).
Hewlett, P. S. & Parkin, E. A., 122.
Hill, M. A., 117.
—— & Roberts, E. W., 118.
Hoare, C. A., 76.
Hocking, K. S., 72.
Höring, R. O., 28.
Huang, K. W. & Mao, Y. C., 75.

Innes, J., 33.

Jacobs, L., 80.
Jansen, G., 95.
Jenkins, D. W., 120.
Johnson, H. A. & Goodman, W. L., 45.
Johnstone, R. D. C., 101.
Jones, W. R., 76.

Kalra, S. L., 70.
Kamal, A. M. & Abdel Messih, G., 38.
——, Anwar, M., Abdel Messih, G. & Kolta, Z., 85.
Katzenellenbogen, I., 55.
Khaw, O. K., 92.
Kikuth, W. & Mudrow, L., 47.
Kirby, H., 117.
Kodicek, E., Carpenter, K. J. & Harris, L. J., 104.
Krantz, J. C., Jr. & Evans, W. E., Jr., 52.

Lambrichts, G. P., 124.
Langeron, M., 111.
Larsh, J. E., Jr., 98.
Lasnier, E. P., Ardao, H. A. & Cassinelli, J. F., (93).
Latner, A. L., Coxon, R. V. & King, E. J., 96.
Lebon, J., Maire, R., Duboucher, G. & Claude, R. (33).
Lemke, R., 62.
Lichtman, J. A., 112.
Lie Kian Joe, 99.
Link, V. B., 43.
Lopes, C. F., 87.

Macchiavello, A., 109.
Macdonald, G., 124.
MacDougall, M. S., 26.
Maciel, P. & Rosenfeld, G., (55).
Mackenzie, M., 57.
de Magalhães, O., 109.
Mani, 74.
Manson-Bahr, P., 76, 83, 101.
Marshall, P. B., 49.
Mateo Alonso, A., 29.
Mathieu, M., 22.
Mayer, M., Pifano C. F. & Medina, R., (54).
de Meillon, B. & Gear, J., 119.
Moiser, B., 91.
Monnerot-Dumaine, M. & Sananes, N., (30).
Morenas, L., 94.
Morris, R. M., 122.
Morton, T. C., 76.
Muniz, J., 54.
——, Nobrega, G. & da Cunha, M., 55.
Murgatroyd, F., 76.

Nagendra, S., 41.
Napier, L. E., 76, 79, 101.
Nascimbene, A. & Prezioso, A., 22.
Nature, 52.
Negroni, P., Fernández, L. L. & Daglio, C. A. N. 110.
Nelson, M. G., 30.
Nieto Caicedo, M., 24.

O'Connor, R. J., 76.
Oldroyd, H., (119).

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Pak, C., 96.
Paraense, W. L., 47.
Parekh, J. G. & Boghani, B. P., 36.
Parkinson, T., 82.
Paterson, A. R., 124 *bis*.
Paul, J. H. & Bellerive, A., 23.
Pavlov, P., (56).
Pérez, J. C., 104.
Pesigan, T. P., Torres, L. F., Jr. & Recio, P. M., (97).
Peus, F., 26.
Pinto, C., 53.
Pinto, G. de S., (32).
Potts, W. H., 51.

Rao, V. V. & Ramakrishna, V., 41.
Raynal, M. J. H., 59.
Reddy, D. J., 71.
Rees, C. W., Reardon, L. V., Jones, F. E. & Griffin, A. M., with Bartgis, I. L., 79.
Reimann, H. A., 74.
Reynes, V., & Delbove, P., 61 *bis*.
Rigdon, R. H., 49.
Rivero, M. D., 50.
Rogers, L., 101.
Roman, E., 55.

Sapero, J. J., 32.
Sautet, J., Audouin, A., Levavasseur, G. & Vuillet, J., 45.
Sayago, G., 91.
Schujman, S., 92.
Schwetz, J., 115.
Shepard, C. C., 71.
Shun-Shin, M., 84.
Shute, P. G., 21.
da Silva, L. C. T., 95.
Simeons, A. T. W. & Chhatre, K. D., 39.
Singer, J., (86).
Southern Rhodesia, 122.
Stannus, H. S., 76.
Stewart, G. T., 76.
Suarez, R. M., (107).
Surraco, N. L. & Galeano Muñoz, J., (98).
Swellengrebel, N. H., 74.

Tarzwell, C. M., 46.
Temkine, M., (30).
Thompson, R. H. S. & Whittaker, V. P., 57.
Thomson, K. J., Freund, J., Sommer, H. E. & Walter, A. W., 49.
Tompkins, V. N. & Miller, J. K., 84.
Topciu, V., (87).
Trans. Roy. Soc. Trop. Med. & Hyg., 76.
Turner, T. B., McLeod, C. & Updyke, E. L., 89.

van Ufford, W. J. Q., (108).

Valdes Ruiz, M. & Salar Luis, E., (98).
Vanderplank, F. L., 51.
van der Scheer, J., Bohnel, E. & Cox, H. R., 60.
Veeraraghavan, N., 19.
Vogel, H., 93.

Waddell, M. B. & Taylor, R. M., 72.
Wannoni, L. L., 126.
War Office, 62.
Wei, H. & Wei, W. P., 62.
Wenrich, D. H., 116.
Wenyon, C. M., 76, 101.
Wexler, L., Adams, H. V. & Goldberg, L. C., 27.
Wharton, D. R. A., 103.
Williamson, J. & Lourie, E. M., 48.
Woke, P. A., 119.
Wu, K., 97.

Yanniceli, R., Suarez, H. & Castro Casal, E., 98.
Yen, C. H., 75.

Zanetti, V., 91.